A STUDY ON ANALYSIS OF VALIDITY OF URINARY CALCIUM AND CREATININE RATIO AS A SCREENING TEST FOR PRE-ECLAMPSIA

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CERTIFICATE

This is to certify that the dissertation titled "**A STUDY ON ANALYSIS OF VALIDITY OF URINARY CALCIUM AND CREATININE RATIO AS A SCREENING TEST FOR PRE-ECLAMPSIA**" submitted by

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INTRODUCTION

INTRODUCTION

Pregnancy usually induces happiness but at times can also induce hypertension. Hypertensive disorders represent the most common medical complication of pregnancy. It complicates up to 7-10% of pregnancies of which pre-eclampsia / Eclampsia constitutes 70%, and Chronic hypertension 30%. Pre-eclampsia has been recognized as pathological entity since the time of Hippocrates and ancient Greeks.

Pre-eclampsia complicates approximately 5 - 8% of pregnancies and is a major cause of maternal and perinatal morbidity (SIBAI et al, 1997, 5-8% ACOG 2002).

Pre-eclampsia and Eclampsia contribute 12% of all maternal deaths in the developing countries (WHO 1999).

It is said that pre-eclampsia, eclampsia contributes to death of a women every 3 minutes worldwide. Infants of women with severe Pregnancy induced hypertension has 5 fold increase in mortality compare to infants of normotensive women.

Pre-eclampsia is a multiorgan disorder, and usually recognized by new onset of hypertension and proteinuria appearing in the second half of pregnancy.

Hypertensive disorders complicating pregnancy represent one facet of a complex disease process. Gestational hypertension, pre-eclampsia, eclampsia majority of these conditions are preventable.

This has led to the interest in screening. Screening the deliberate examination of substantial segments of the population in search for disease at its earlier stages, is a logical extension of the role of preventive medicine. If we wish to prevent such disorder we must seek ways of preventing (or) ameliorating the disease process. In preventing this disorder the most important factor is lack of timely prediction.

Several methods have been proposed to identify the pregnant women who are at risk for pre-eclampsia. Renal function changes in pre-eclampsia which has been documented and several prospective studies indicate that atleast some of the changes are present before the clinical diagnosis of pre-eclampsia. One such change is the association of hypocalciuria with pre-eclampsia as early as 24 weeks.

The purpose of this study is to predict the development of pre-eclampsia in symptom free pregnant women using urinary calcium/ creatinine ratio (UCCR), For a screening test to be of value, it should be selective, reliably cheap and easy to perform. It should increase the predictive value and the prophylactic measures must be effective.
Good antenatal supervision followed by appropriate treatment will definitely help mother and baby for good outcome.

REVIEW OF LITERATURE

Pregnancy can induce hypertension in normotensive women (or) aggravate already existing hypertension. Hypertensive disorder in pregnancy continues to take heavy toll of maternal and fetal lives.
Pre-eclampsia, eclampsia remains a difficult puzzle to solve, and it is still in a cloud of mystery.

HISTORICAL PERSPECTIVE OF PRE - ECLAMPSIA

Zweiff first termed pre-eclampsia as "Toxemia"
Zweiff & Chesley called it is disease of theories probably, the oldest reference is the **Athvaida - Veda** 200 BC.
Fishberg (1899) - Pre-eclampsia as a cause of essential hypertension.
Lever And Simpson 1843 - Discovery of proteinuria in pre eclampsia.
Lahlein 1918, Fahr 1920 - Significant changes in the glomeruli.
Farguhar 1959 - demonstrated glomerular capillary endotheliosis by electron microcopy.

INCIDENCE

Incidence of pre-eclampsia in commonly cited to be about 5%. Incidence is influenced by parity, race and genetic factors. (Women with positive family history of pre-eclampsia in her mother or in her sister).
In India the incidence of pre-eclampsia amongst hospital patients is about 7-10% of all antenatal admission. In United Kingdom, the incidence is 10%. In USA it is 6-7%. The incidence is found to be higher among nulliparous women, age less than 20 years and more than 35 years.

DEFINITION

Gestational hypertension or Transient Hypertension, previously called as Pregnancy Induced Hypertension.
A diastolic BP of 90mmHg (or) higher (or) a systolic BP level of 140mm Hg or higher for the first time during pregnancy after 20 weeks of gestation in a women with previously normal blood pressure but in whom proteinuria is not developed (NHBPEP 2000; ACOG 2002).

PRE-ECLAMPSIA

Pre-eclampsia is a pregnancy specific syndrome of reduced organ perfusion secondary to vasospasm and endothelial activation.

INTERNATIONAL SOCIETY FOR STUDY OF HYPERTENSION IN PREGNANCY

(Davey and MacGillivray 1988) (ISSHP)

1. One measurement of Diastolic BP equal (or) >110mm Hg
2. Two consecutive measurement of diastolic BP=/>90mm Hg, 4 (or) more hours apart.
3. Korotkoff's V sound is to be measured for measuring diastolic component.

A Diastolic Blood Pressure of 90mm Hg after 20 weeks of pregnancy is usually considered the threshold for diagnosis. A diastolic pressure of 90mmHg is 3SD greater than mean for mid pregnancy

and 2SD above the mean for 34 weeks gestation. 1.5 SD above mean at term, reflecting the physiological increase in blood pressure towards term (MACGILLIVRAY et al, 1969).

BLOOD PRESSURE MEASUREMENTS

1. Conventional mercury sphygmomanometer - **Gold standard** for blood pressure measurement.
2. Use of bell of stethescope as it better amplifies the Korotkoff (K) Sound.
3. Cuff size should be adequate. Bladder length 80% of arm circumference, and width should be 40% of arm circumference.
4. Patient should be in sitting posture with her right arm well supported in a horizontal position at the level of heart and her feet supported ***(Sibbai)***.
5. Inflate the cuff above the systolic pressure as recognized by disappearance of the radial pulse.
6. Use of Korotkoff (V) (disappearance of sound) to determine diastolic blood pressure.

CLASSIFICATION

NATIONAL HIGH BLOOD PRESSURE EDUCATION PROGRAMME WORKING GROUP (2000) (NHBPEP)

I. Gestational Hypertension

Gestational Hypertension or transient Hypertension, Previously called as Pregnancy Induced Hypertension.

- > 140/90 mmHg of BP for the first time in pregnancy.
- No proteinuria
- Blood pressure returns to normal < 12 weeks postpartum
- Final diagnosis made only postpartum.

II. Pre Eclampsia

Occurrence of Hypertension in combination with proteinuria developing after 20 weeks of gestation in a previously normotensive, non proteinuric pregnant women.
It is a pregnancy specific syndrome of reduced organ perfusion secondary to vasospasm and endothelial activation.

Minimum criteria	*Increased certainity of Pre eclampsia*
❖ ≥140/90 mm Hg >20 weeks of gestation ❖ Proteinuria ≥ = 300mg/24 hrs (or) ≥ = 1 + dipstick	❖ Blood Pressure ≥ = 160/110mmHg ❖ Proteinuria 2g/24 hours (or) ≥=2+ dipstick ❖ Serum Creatinine 1.2mg/dl unless known to be previously elevated ❖ Platelets <1,00,000/mm^3 ❖ Microangiopathic haemolysis ❖ Elevated ALT/ AST ❖ Persistent headache/ Other cerebral or visual disturbances ❖ Persistent epigastric pain.

III. Eclampsia

Seizure that cannot be attributed to other cause in a women with pre-eclampsia.

Superimposed Pre-eclampsia on Chronic Hypertension

New onset proteinuria > 300 mg/24 hours in hypertensive women but proteinuria before 20 weeks of gestation.

Chronic Hypertension

BP ≥ 140/90 mmHg before pregnancy or diagnosed before
20 weeks gestation not attributable to gestational trophoblastic disease.

Proteinuria

It is directly proportional to maternal and perinatal mortality, **(Harth et al 2000)** and morbidity.
It is an important sign of pre eclampsia **(Chesley 1985)**. It reflects the glomerular damage that causes leakage of proteins through the basement membrane.
Significant proteinuria is defined by 300mg/24 hours or persistent 30mg/dl (1+dipstick) in random clean catch sample on at least 2 occasions collected 6 hours apart. If proteinuria is >5gm/24 hours (or) persistent 3+ dip stkck (or) more the condition is called as severe pre eclampsia (ACOG Practice Bulletin No.33, January 2002).

Edema

Edema is no longer a part of current definition (or) as a diagnostic criteria of pre- eclampsia **(Williams 22nd Edition)** and it is seen in nearly 80% of women in last few weeks (Robetson 1971).

Weight Gain

Excessive weight gain of >0.5kg/week because of extracellular fluid volume expansion.

THEORIES REGARDING CAUSATION OF PRE-ECLAMPSIA

IMMUNOLOGICAL

The trophoblastic cells do not express the usual class-I & II MHC antigen, they express unique HLA-G enclosed class-I MHC molecule which allow the trophoblast cells to invade deep into spiral arteries. In patients developing pre-eclampsia there is immune resistance to the invading trophoblast by the maternal immune system, results in poor spiral artery remodeling which is a initially cited feature in pre-eclampsia **(ZHOU 1977).** Pre-eclampsia is immune mediated, certainly the microscopic changes at maternal placental interface are suggestive of acute graft rejection ***(Labarrere 1998)***.
The risk is enhanced when formation of blocking antibodies to antigenic sites in placenta is impaired ***(Bardegue and Asso, 1991)*** (or) where the number of antigenic sites is increased as in hyperplacentosis ***(Beer 1979)***.

- T helper cells were in a lower proportion in pre-eclampsia ***(Bardeguez and Associates)***. T-lympohcyte secrete cytokines that promote implantation and their dysfunction may favour pre-eclampsia ***(Hayashi & Associates 2004, Whitecar & Collegues 2001)***.
- Antibodies to B2 glycoprotein I is more relevant immune complex and antiendothelial antibodies may be involved ***(Taylor et al., 1999)***.
- Immunocytochemical analysis - VCAM, increased in Pre-eclampsia.
- The pre-eclampsia develops more frequently in multiparous women impregnated by a new Consort (Mostello & Conera 2002, Trapin and Colleagues 1996).

GENETIC SUSCEPTIBILITY

Hereditary estimate of 31% of pre-eclampsia (Nilsson et al)

1. ***Chesley and Cooper 1986***, Pregnancy Induced Hypertension is inheritable both by single gene (Broughton Piplus 1999) and Multifactorial inheritance.

   2 Modes

   a) Simple recessive model with genes acting in the mother (gene on chromosome 1, 3, 9)
   b) Dominant model with incomplete penetration
2. ***Kilpatric*** reported an association HLA DR4
   The transmission from mother to daughter is through $HLADR_4$
3. Angiotensinogen gene variant T235 - high incidence of PIH **(Arngrimsson et al)**
4. Dizon Townsend and colleagues found high incidence of factor V laden mutation polymorphism gene variant 202109
5. Epigenetic features (or) imprinting is also involved in the pathogenesis of pre-eclampsia susceptibility locus on chromosome 10q 22-1. **(Dudejans et al).**
6. Hyperhomocystinaemia associated with methyltetrahydrofolate (6778) Homozygozity **(Coffer et al).**
7. Polymorphism of TNF α and Gene - Mediating endothelial dysfunction, Lymphotoxins, IL_1.
8. The eNOS gene susceptibility occurs in the region of chromosome 7q 36.

ENDOTHELIAL DYSFUNCTION

- Endothelial damage account for all aspects of pathophysiology of pre-eclampsia ***(Roberts et al 1998).***
- Endothelial dysfunction results from "Generalised perturbation of normal maternal intravascular inflammatory adaptation to pregnancy ***(Redman and Colleagues (1999).***
- Immunologically mediated deficiency in trophoblastic invasion of spiral arteries results in release of a number of factors into maternal circulation. These changes inturn provoke activation of vascular endothelium ***(Hayman and Asso., 2000, Ness and Roberts 2000, Walker 2000).*** Damaged endothelium activates endothelial cells to promote coagulation and increases sensitivity to vasopressor agents.
- Reduction of unbound serum level of Angiogenic factors such as VEGF and PLGF due to upregulation of soluble fms like tyrosine kinase receptor **(Maynard et al)** and Serum level of sFlt1 is increased in pre-eclampsia leads to endothelial dysfunction ***(Luttun and Carmeliet 2003).***
- Recent study - increased level of asymmetric dimethyl arginine at 23-25 in pregnant women who is at risk of
  pre-eclampsia (important in nitric oxide cyclic guanosine monophosphate pathway).
- Prostaglandin theory (Wang et al 1991): In pre-eclampsia, the balance is between PGI2 & TXA2 (Prostocycline) (Thromboxane A2) is titled so TXA2 is found to increased ***(Walsh 1985)***.

ENDOTHELINS

They are polypeptides with potent vasoconstricting property, higher level of Endothelin I is found in pre-eclampsia ***(Clark Schiff 1992)***.

NITRIC OXIDE

- Decreased in pre-eclampsia ***(Anumba Ford Am obsgyn 181: 14 (1999)***. This concept is disproved. Decreased endothelial nitric oxide synthase expression (Wang & Collagen 2004). Increased production of Nitricoxide as a compensatory mechanism **(Benedetto & Asso., 2000)**. It is a consequence of hypertension, but not the cause **(Morris and Colleagues 1996)**.
- Ionic calcium is crucial for synthesis of vasosubstances in the endothelium like PGI2 and Nitricoxide. An alteration in the action of Nitricoxide may be related to inactivation by free radical superoxide (secondary to inflammatory process) ***(Lopez et al)***.

DIETARY DEFICIENCY

Role of dietary deficiency in the pathogenesis of pre-eclampsia **(Mac Gillivary et al)** Calcium concentration low in extracellular fluid, amount of ionic calcium entering the cell was increased making smooth muscle more sensitive to excitability ***(Ganong 1979).***
Serum calcium decrease in pre-eclampsia (Dawson, Kelly and Co-authors Biological Trace element research May 2009 - Page: 107-116). An inverse relationship was found to be associated to serum calcium and incidence of pre-eclampsia (Sanders Sarks, Appel J of HT Dec 1995).
Belzian and Collegeues (1998): They reported that after mid pregnancy dietary supplementation with 2 grams of elemental calcium/day significantly reduces the Incidence of pre-eclampsia.

OXIDANTS AND ANTIOXIDANTS

A work by **Hubal et al** have confirmed that pre-eclampsia may have its origin in a disturbed oxidation

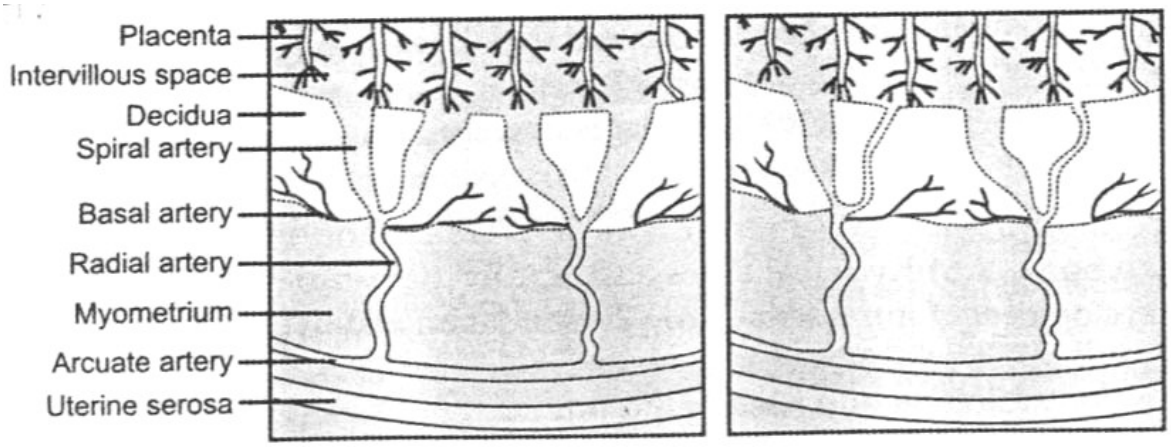
mechanism. Increased free radical in Pre-eclampsia (Wisdom and Ass., 1991), free radical causes endothelial damage.

PLACENTAL PROTEINS

Corticotrophin releasing factor, HCG, Activin A & inhibin A are said to play a role in pathogenesis of Pregnancy induced hypertension.

- ❖ Decreased intravascular volume
- ❖ Decreased glomerular filtration rate

VASOSPASM



Showing physiological distension of spiral arteries in deciduas (left)

and it absence in Pre eclampsia (right)

Vasopasm that characteristic of the disease (Volhard). Vasopasm causes endothelial damage and interendothelial cell leakage which results in subendothelial deposition of fibrin and platelets and hence uteroplacental insufficiency (Brunner & Gavras 1975).

PREDISPOSING FACTORS

AGE

Young primi <20 years of age and all patients >30years of age are said to have increased chance of pre-eclampsia **(Bobrowski & Bottoms 1995)**.

PARITY

Primigravida are 15 times more affected than multigravida. The incidence among primigravida is 11.9% and multiparity is 4.7%. The incidence is 24% in new paternity because of shorter period of sperm exposure proceeding conception.

CPEP - Calcium for Pre-eclampsia Prevention study shows significant risk for development of pre-eclampsia in Nulliparity, specially noted at index visit

1. Body Mass Index Odds ratio 3.22 or = 35kg/m^2 Vs 19.8kg/m^2
2. Systolic blood pressure odds ratio 2.66 for >or=120 Vs <101mmHg.
3. Diastolic blood pressure odds ratio 1.72 for > or = 61mmHg Vs 60mmHg.

SOCIO-ECONOMIC STATUS

(BASRD and Colleagues 1969) incidence not different among socio economic classes.

FAMILY HISTORY

Inheritance is 3 times if present in 1st degree relatives.

Chesley has reported an incidence of 26% in daughters and 8% in daughter in law. Mendelian recessive trait is more acceptable.

WEIGHT

Risk of pre-eclampsia is progressively increasing from 4.3% for women with body mass index less than 19.8 Kg/m^2 to 13.3% for those greater than (or) equal to 35 kg/m^2.

OBESITY

Adipocytes lead to the formation of cytokines especially TNFα - which exacerbates of underlying essential hypertension.

TWINS

13 versus 5% due to superabundance of trophoblastic tissues (Simbai & Co-workers)

DIABETES MELLITUS - 30%

HYDATIFORM MOLE

Confined to large rapidly growing moles in which the incidence of pre-eclampsia is 70% (Page 1939).

HYDROPS FOETALIS

Pre-eclampsia is due to hyperplacentosis

DIETARY DEFICIENCY

Deficiency of calcium associated with increased incidence of pre-eclampsia.

CLIMATE

In cold weather - increased peripheral vasoconstriction.

Renal disease 20% of pre-eclampsia can occur
Thrombophilias - Uteroplacental thrombus is frequently seen in pre-eclampsia (Dekkar 2003).

RECURRENCE

25 - 50% women had recurrence in their subsequent pregnancies.

Pre-eclampsia	: 45.5%
Eclampsia	: 1.4 %
Abruption	: 2.5%
HELLP syndrome:	3%

SMOKING

Significant reduction in level of HCG and Estradiol level due to direct effect on the placental function (***Bernstein et al 1989***). Smoking reduces the incidence of pre-eclampsia.

HIGH RISK FACTORS FOR PRE-ECLAMPSIA (ADAPTED FROM DUCKITT AND HARRINGTON 2005 AND DEKKAR ET AL 1995)

Maternal related factors

1. First pregnancy
2. Extremes of age
3. Pre-eclampsia in a previous pregnancy
4. > 10 years since previous pregnancy
5. >40 years of age
6. Body mass index > 35 at booking
7. Family h/o. Pre-eclampsia (Mother (or) sister)
8. Diastolic BP >80 mm Hg at booking
9. Proteinuria at booking
10. Multiple pregnancy
11. Underlying medical condition.
12. Obesity
13. Thrombophilia
14. Auto immune disorders

Paternity related factors

1. Primi paternity
2. Limited sperm exposure
    i. Donor insemination
    ii. Oocyte donation
3. Partner who fathered a pre-eclampsia pregnancy in another women.

Pregnancy associated factors

1. Multiple pregnancy
2. Hydropsfoetalis
3. Chromosomal anomalies
    a. Trisomy 13
    b. Triploidy
4. Hydatiform mole

PATHOPHYSIOLOGY

PRIMARY LEVEL

The presence of fetus is not necessary for pre-eclampsia to occur. But a placenta is an absolute must. Uteroplacental circulation is unique, it lacks a micro circulation.
Two lesions that involve spiral arterioles, which are the end arteries supplying Intra vascular space **(Redeman 1991)**.

i) **Deficient placentation -** In normal pregnancy - spiral artery remodeling by trophoblastic invasion between 8 and 15 weeks of gestation so as to transmit the expanded blood volume after 20 weeks of gestation. So failure of trophoblastic invasion results in failure of the vessels to dilate and responds to vasoconstrictor stimuli resulting in decreased choriodecidual blood flow **(Dixon and Robertson et al).**

ii) Acute atherosis ***(Robertson et al 1963, Laberrere C)*** it is a late pathological occurrence. Lipids accumulates first in myointimal cells and then in macrophages **(Madzali & Colleagues, 2000).**

The dual pathology of the spiral arteries explains reduced placental flow and desaturation of the intervillous space. These changes are consistent with the maternal signs of pre-eclampsia.

Oxidative stress

At present, the most popular theory is ***"Oxidative stress".***

Reduced placental perfusion where prooxidants dominate over the antioxidants results in formation of free radicals. Imbalance between free oxygen radical and scavengers is in favour of oxidative stress. Oxidative stress leads to increased production of lipid peroxides, TXA2 and decreased level of prostacyclin (PGI_2). This imbalance triggers endothelial dysfunction and its clinical manifestations. Recently decreased expression of reducing system like thioredoxin and glutaredoxin in placenta in a pre-eclampsia patients have been documented. Greater accumulation of 4- hydroxyl - 2 non renal (HNE) modified renal proteins which are markes for lipid peroxidation in the placenta of pre-eclampsia.
In pre-eclampsia, increased production of nitric oxide, as a compensatory process, this nitricoxide competes with superoxide dismutase and combine with super oxide which is formed by reduction of oxygen to form peroxynitrite which has got toxic effect.

SECONDARY

Results from maternal adaptation to Ischemic placenta.

CARDIOVASCULAR SYSTEM

1. **Haemodynamic change**
   a. Increased arterial sensitivity to Angiotensin II
   b. Increased peripheral resistance
   c. Decreased cardiac output
   d. Increased blood pressure
2. **Blood volume**
   a. Hemoconcentration is a hall mark of eclampsia
   b. Reduced circulating blood volume in women homozygous for T_{235} angiotensin gene type associated with pre-eclampsia **(Silver & Asso., 2001).**

RENAL SYSTEM

1. Reduced uric acid clearance
2. Reduced glomerular function
3. Reduced renal blood flow
4. Intrinsic renal changes **(Pritchard & Colleagues 1984)**
5. Proteinuria **(Naeye & Friedman 1979, Meyer & Colleagues 1994)**
6. Glomerular endotheliosis **(Spargo et al 1959)**
   Glomeruli were enlarged by about 20% **(Sheehan 2001)**
7. Immunofluorescent staining identified fibrinogen changes **(Lichtig et al 1975)**
8. Urinary sediment - reflects renal changes **(Ledou et al)**
9. Reduced urate clearance **(Chesley and Williams 1945)**
10. Hypocalciuria **(Taufield et al 1987):** Pre-eclampsia is associated with the diminished urinary excretion of calcium because of increased tubular reabsorption.
11. Hyperuricaemia **(Pollate et al 1960)**

COAGULATION SYSTEM

1. Intravascular coagulation **(Baker and Lunningham)**
2. Thrombocytopenia, Platelet aggregation is reduced **(Baker and cunningham 1999).** Lower the platelet count, higher the maternal and fetal morbidity and mortality **(LEDUC 1992)**
3. Fragmentation Haemolysis **(Sanchez Ramos and Colleagues 1994).** Increased erythrocyte membrane fluidity in women with HELLP syndrome.
4. Anti thrombin III - reduced **(Chang and Co-workers 1992)**
5. Fibronectin - elevated **(Bru baker and Colleagues 1992)**
6. Increased fibrinopeptide A.

HEPATIC SYSTEM

1. Elevation of liver enzymes **(Combes and Adams 1972)**
2. Increased hepatic artery resistance in Doppler sonography **(Ooster Hof and Co-workers 1994)**
3. HELLP syndrome - haemolysis, elevated liver enzymes & Low platelets.

ENDOCRINE SYSTEM

1. Atrial natriuretic peptide - increased in women with pre-eclampsia (Gallery and Lindheimer 1999)
2. Increased plasma level of renin angiotensin.

TERTIARY

The systemic upsets of pre-eclampsia can eventually progress to decompensation which presents as one

of the possible causes.
Tertiary pathology of pre-eclampsia

- Eclampsia
- Cerebral haemorrhage
- Cerebral odema
- Pulmonary edema
- Adult respiratory distress syndrome
- Retinal detachment
- Laryngeal odema
- Dissiminated intravascular coagulation
- HELLP syndrome
- Renal cortical necrosis
- Hepatic rupture

CALCIUM

Calcium is the fifth most common element and most prevalent cation in the body. It makes up 1.2-2% of body weight. The total body calcium content is 1000 - 1500 grams, 99% of this incorporated in bone where it exist as carbonates and phosphates and rest is found in extra cellular fluid.

SERUM CALCIUM

Normal serum calcium level ranges from 9.0-10.5mg/dl (2.2-2.6 mmol/L). About 45% of total calcium is in ionized form. Albumin is a major protein in which non - diffusible calcium binds. Ionized calcium is the physiologically active form. A decrease in serum albumin of 1g/dl results in decrease of about 0.8mg/d in total serum calcium. Calcium exist in ionized form in extracellular fluid and regulates action on kidney, intestine and bone.

ABSORPTION

Absorbed in jejunam and duodenum against electric and concentration gradient. Absorption increased in acidic medium. Absorption requires 1,25 dihydroxy cholecalciferol. Major portion of filtered calcium is reabosorbed by hormone dependent mechanism in proximal convoluted tubule. Calcium hemostatic mechanism resides in convulted tubule of kidney.

EXCRETION

Excreted in faeces, urine and sweat. 130 mg/day calcium is excreted through faeces, 2-4 mg/kg/day via urine, 15mg/day of calcium is excreted in sweat.
Foetal calcium correlate with intake. The presence of phosphorous decreases calcium excretion.

REGULATION

The normal serum calcium is maintained by integrated actions of Parathyroid Horome (PTH) and vitamin D metabolites, calcitonin, cytokines such as transforming growth factor B and interleukin 6 **(Am J Clin Nutr 2004;80;417 - 20)**
25 - Hydroxy cholecaliferol gets converted to active form 1, 25 dihydroxy cholecalciferol in proximal convuluted tubule in kidney where 1 α hydroxylase enzyme is present. 1, 25 dihydroxy cholecalciferol is a important hormone acts on gut and kidney to reabsorb calcium. Paratharmone is a major hormone, any fall in ionized calcium countered by secretion of paratharmone which acts on bone causing bone resorption, in the kidney it acts on the distal tubule causing calcium reabsorption and through stimulation of vitamin D3 which increases calcium absorption from intestine, reabsorpition from kidney and mobilization from bone. All these help to increase the calcium level and achieve an optimum level in serum. 1, 25 dihydroxy Vitamin D is reduced in pre-eclampsia because of placental hypoperfusion and renal damage **(Serner et al 1981)**.

CALCIUM IN NORMAL PREGNANCY AND PRE-ECLAMPSIA

Because of substantiate foetal needs 300mg/ day and as well as increased renal calcium excretion from augmented glomerular filtration. The concentration of total calcium in maternal serum gradually declined during pregnancy reaching a nadir during the III trimester and rising slightly thereafter PTH levels were assumed to be increased in pregnant women, (However seeley and co-worker 1997 reported a significant in intact PTH level during pregnancy) and lower biological activity of parathyroid hormone. At the same time they showed a two fold increase in serum concentrate of 1, 25 dihydroxy Vitamin D, which is probably of placental and decidual origin. It enhances gastrointestinal absorption of calcium to meet the needs of pregnancy.

Loper et al had shown that women with pre-eclampsia have significant decrease in level of serum ionized calcium. Total serum calcium level decline parallel to decreased serum albumin concentration (Power and amaises 1999) Importantly however ionized calcium levels are unchanged in normal pregnant women (Dahlman and Colleagues 1994). But serum ionized calcium is lower in pre-eclampsia, at the same time intracellular concentration of ionized calcium is greater in patients with pre-eclampsia ***(Pereyra et al, 1991)*** and decreased calcium dependant ATPase activity of erythrocytes and hypocalciuria.

HYPOCALCIURIA

The urinary calcium excretion in normal pregnancy is 350-620mg/day compared with 100-250mg/day in non pregnant women.

The pathophysiology of hypocalciuria in pre-eclampsia patient is not well understood. Reduced urinary calcium excretion may be the result of dietary, renal and hormonal factor. During pregnancy calcium transported from maternal blood across the placenta, therefore increased calcium uptake by placenta may result in maternal hypocalciuria.

In pre-eclampsia, there is reduction in calcium 1, 25 dihydroxy Vit.D which enhances the PTH, there is reduced placental perfusion with renal damage, this lead to decreased synthesis of active form of Vit. D, which would stimulate PTH and thereby increases distal renal tubular as well as proximal tubular level of reabsorption of calcium resulting in hypocalciuria. Vasoconstriction resulting from low calcium which causes decrease in glomerular filtration, increased tubular reabsorption of calcium and diminished urinary calcium excretion. Urinary calcium excretion is inversely related to the incidence of pre-eclampsia.

Rodriguez et al, have found 24 hour urinary calcium excretion was lower in preeclamptic patients than in the normotensive group in his recent studies and also he evolved the value of calcium/ creatinine ratio as predictive test using value of < 0.04µg/ml.

Weiss et al, study says that, in pre-eclampsia the fetus is exposed in utero to toxemic environment, its kidney function may be similarly affected. So there may be higher aminiotic fluid divalent cation concentration due to maternal hypocalciuria.

Many studies on the urinary calcium excretion have been performed.

Ye-Y; Dai.S, Gng-Xi et al., at Quindo Medical College, predictive value of urine calcium measurement on occurrence of Pregnancy induced hypertension gives a predictive value of urinary calcium/ creatinine ratio in 24 hour urine sample. The values were significantly lower than that of in normal pregnant group (P <0.01) 3mmol/ of urinary calcium concentration and 0.04 of calcium creatinine ratio with sensitivity of 76.2% and specificity of 97.5%. They conclude the lower urinary calcium excretion is valuable marker.

Taufield PA (1987): Pre-eclampsia is associated with hypocalciuria due to increased tubular reabsorption of calcium. He measured 24 urinary calcium excretion and found low total and fractional excretion in women with pre-eclampsia, when compared to normotensive women. The urinary calcium concentration ≤ 12mg/dl in 24 hours collection has positive and negative predictive value of 85% & 95% respectively for the diagnosis of pre-eclampsia.

Sanchez-Ramos.L (1991): determination of low - urinary calcium creatinine ratio in a single voided urine sample is accurate as a 24 hours collection. This phenomenon occurs early in pregnancy and persists throughout gestation and it is useful for the early identification of patient at risk.

Suzuki Y. Hayashi (1992): concludes that urine calcium / creatinine ratio was significantly lower in women with pre-eclampsia than in healthy pregnant women.

Ozcan T (1995): UCCR < 0.04 predicts development, of PE in later pregnancy. This study suggests that a single urinary calcium / creatinine ratio might be an effective marker for predicting pre-eclampsia in a high risk population.

Saudan PJ & Shaw L (1998): in American Journal of Hypertension States: Gestation hypertensive patients who became preeclamptic had lower urinary calcium / creatinine ratio than women whom remained gestational Hypertension. This test had a sensitivity of 68% and specificity of 70%. This low value preceeds the emerging of pre-eclampsia by 12 days.
Kar et al (2002) of Goralehpur and **Desai et al (2001)** from Barod: Role of urinary calcium / creatinine ratio in first morning urine in the mid trimester of pregnancy for predicting risk of PIH. The ratio <0.04 is predictive of increased risk of pre-eclampsia. A ratio of > 0.04 predicted a 96% chance of not developing pre-eclampsia.
Serum creatinine concentration varies with glomerular function of creatinine clearance. So even the small changes in glomerular function are best detected by creatinine clearance.

HYPERTENSION

Evidence supporting an inverse relationship between calcium intake and blood pressure has strengthened in the past decade, low calcium intake may cause high blood pressure by stimulating release of PTH and (or) renin thereby increasing intracellular calcium in the vascular smooth muscle causing vasoconstriction. Extra cellular ionized concentration is crucial for the production of nitricoxide and regulation of vascular sensitivity. Vasoconstriction causes decrease Glomerular filtration rate (GFR), increased tubular reabsorption of calcium and diminished calcium excretion. Calcium supplementation has been reported to reduce the incidence of pre-eclampsia **(Repke & Villar 1990).**

Different studies have been performed to study the relationship between calcium, metabolism and hypertension

Smolarczy K.R. et al: Patient with Pregnancy Induced Hypertension due to renal impairement there is reduction of urinary calcium excretion and calcium concentration in blood.
Prada JA et al: Pregnancy induced hypertension produced by low calcium diet lead to significant increase in maternal blood pressure vascular resistance.

The role of calcium to prevent Pre-eclampsia is as follows

I. High dose of calcium exert a negative feed back

effect on parathyroid hormones

↓

Lowering intracellular calcium ion levels

↓

Smooth muscle relaxation and diminished

responsiveness to pressor stimlus.

II. Further more calcium supplementation is associated with higher levels of calcium excretion which is coupled with an ion exchange with magnesium resulting in increased level of magnesium

- smooth muscle relaxation in vessels → control of hypertension

(Belzian et al 1998).

SCREENING TEST

Comparison of various other screening tests with urinary calcium / Creatinine ratio as a predictor of Pre-eclampsia.

A variety of biochemical and biophysical markers based primarily on rationales implicated in the pathology and pathophysiology of pre-eclampsia have been proposed for its prediction.
The good screening test should be sensitive, cheap, easy to perform, and readily interpretable with high predictive value.
Screening test can be divided into 3 categories.

I. Haemodynamic Tests

1. Angiotension II infusion test: Talledo et al 1968

Abnormal vascular reactivity of patients destined to develop pre-eclampsia may be detected several weeks before the clinical signs and symptoms appears. Women requiring less than 8ng/kg/minute of Angiotension II to raise their diastolic BP by 20mmHg had a positive predictive value of 20-40% of developing pre-eclampsia **(Friedman)**.

2. Isometric hand Grip Test

Dagani et al Increase in diastolic pressure of more than 20mmHg during a hand grip exercise test at 28-32 weeks had positive predictive value of 20-30%. This test is not affected by positional change and is safe and easily performed, although it is time consuming taking upto 30minutes to perform. Since hand grip represent sympathetic nervous system activity. There is little evidence that pre-eclampsia is mediated by sympathetic activity. This requires further evaluation. False negative 4% & False positive 19%.

3. Roll over test

Proposed by Gant et al, An increase > 20mmHg of diastolic blood pressure induced by having women assume the supine position after lying left lateral position done at 28 - 32 weeks was shown to be associated with later on occurrence of pre-eclampsia is 33%. Though the test is simple to perform and requires only time and personnel rather an elaborate equipment.

4. Mean arterial pressure - Page and Christianson

Suggested that patients with MAP of >90mmHg in II trimester should be regarded as a risk category but the predictive value varies greater from one study to another. The position of the arm relative to heart level also affect the recording. There is also variation of blood pressure with the circadian rhythm, values being highest during the afternoon and early evening. This method to be effective, increased uniformity of recording measurement is necessary.

5. Uterine artery Doppler Velocimetry

Doppler measurement of uterine artery impedance in the mid II trimester (18-24 weeks) is an early screening test **(Bewley, 1991)**, Chappel based on the presumption that impaired trophoblastic invasion of spiral arteries causes decreased utero placental blood flow. The presence of a high systolic - diastolic ratio, persistence of diastolic notch may predict pre-eclampsia (Irion et al 1998) and Resistance Index > 0.58. Positive predictive value was only 28% ***(Friedman and Lindheimer 1999)***. Studies concluded

that the test was not helpful in the management of Individual patient.

URINARY ASSAYS

1. Urinary calcium excretion

Studies found that urine calcium excretion is reduced in pre-eclampsia. A study showed that urinary calcium excretion average of 313±140mg in normal pregnancy and 248±134 in transient hypertension. Hypocalciuria is due to increased distal tubular reabsorption alternatively proximal tubular reabsorption. 24 hour urinary calcium excretion less than 12 mg/ dl had sensitivity of 88% and positive predictive value of 91%. **(Sanchez - Romos, Obstet & Gynecol 1991).**

Another study reported that patient with pre-eclampsia had significantly less excretion of total calcium (129.7 ± 18.7mg/24 hours) than normotensive (283.9 ± 12.3) or those with gestational hypertension (233.2 ± 22.3) (P = 0.0001) using a receiver operator curve, urinary calcium threshold of 12mg/ dl was choosen as a predictor for the development of pre-eclampsia with sensitivity of 83% specificity of 91%, Positive predictive value 83, Negative predictive value 91.

2. Urinary calcium / Creatinine Ratio

A number of studies have shown that a low calcium and creatinine excretion is a valuable marker for pre-eclampsia prediction. Since creatinine clearance is not significantly different among normotensive and pre-eclampsia, (134.4 ± 14.9) in Pre-eclampsia (141.9 ± 7.2) and in gestational Hypertension, (150.2±6.5) in normotensive pregnant women. Studies were done using single voided urinary calcium / creatinine ratio in the prediction of pre-eclampsia and it correlated well with 24 hours calcium excretion. Hence 24 hours urinary calcium excretion can be estimated from single voided urine sample.

Sanchez - Ramos et al., indicate that this phenomenon occurs early and presents throughout gestation being potentialy useful for prediction of pre-eclampsia.

Rodriquez et al., evaluated the value of calcium / creatinine ratio as predictor test using value of < 0.04 µg/ml.

24 hours urinary calcium / creatinine ratio in pre-eclampsia were significantly lower than that of normotensive pregnant women ($p<0.0001$). 3 mmol/L of urinary calcium concentration, urinary calcium creatinine ratio 0.04µg/ml were chosen as predictive threshold for development of PIH with sensitivity of 76.2%, 81.0% and specificity of 97.5%, 98.2% respectively.

Indian study showed spot urinary calcium/ creatinine ratio done in pregnant women between 24-34 weeks of gestation showed that 13.46% had urinary calcium creatinine ratio <0.04. Out of which 71.4% patients developed pre-eclampsia which was found to be statistically highly significant and 80% developed pre-eclampsia with history of risk factors.

3. Micro albuminuria

By Radio immuno assay can detect microalbuminuria of the value >11 µg/ml when done between 24-34 weeks it indicates positive result.

4. Urine Kallikrein / Creatinine ratio

Kallikrein Creatinine ratio of <170 between 16 and 20weeks of pregnancy predicts future development of pre-eclampsia. Camphell et al., 1987: sensitivity of 83% false positive ratio of 50%, false negative ratio 10%, positive predictive value of 91%.

5. Urinary metabolites of PGI_2 - help in diagnosis of pre-eclampsia

6. Markers for endothelial dysfunction

Fibronectin, a glycoprotein synthesized in the vascular endothelium elevated in pre-eclampsia - 2 fold increase in fibronectin, >400 μg/ml. Positive predictive value was only 39% negative predictive value 98% (Chavarria et al, 2003) Sensitivity is quiet low only (69%) **(Pallberg & Colleagues).**
Plasminogen inhibitor 1 is increased relative to plasminogen activator **(Caron and Colleagues 1991)**
Thrombomodulins, cell adhesion molecules and Endotheline I are also found to be increased.

7. Coagulation factors

1) Increased Thromboxane A_2 **(Fitzgerald et al)**. 2) Increased Factor VIII. 3) Decreased Antithrombin III. 4) Thrombocytopaenia and abnormalities platelet function (Aggregation).

8. Cytokines

Increase IL and TNF α - not yet proved sufficiently (Savvidon and colleagues 2002, Benyo 2000).

9. Anti angiogenic factor

Levin RJ et al, soluble fms like Tyrosine Kinase I, Endoglin-Increased, Ratio of sFlt1: PIGF - more accurate (Devivo et al).

MARKERS OF OXIDATIVE STRESS

1. Malondialdehyde lipid peroxidation (Hubel & Co-authors 1989).
2. Pro oxidants (Herbert and Colleagues 1994)
3. Homocysteine (Cotter and Associates 2001) elevated level around mid pregnancy had a 3-4 fold risk of development of pre-eclampsia.
4. Triglycerides, free fattyacids and lipoprotein (Hobel and Colleagues 1996).
5. Prostaglandin Isomerase; marker of impending pre-eclampsia **(Regan and Fitz Gerald, 1997).**

These tests are not economical they are not popularized.

OTHER

1. Uric Acid

Elevated uric acid levels exceeding 5.9 mg/dl is considered significant correlation well with sensitivity and perinatal outcome.

2. Fibronectin

Increased serum cellular fibronectin level in some women with pre-eclampsia (Magann EF et al).

3. Placental peptides

HCG (Ashoc R & colleagues 1997) inhibin A & inhibin B - in the search for early pregnancy marker for pre-eclampsia (Woodruff)

4. Plasma P Selection: Plama P selectin as the earliest predictor in the first trimester is under study.

5. Urinary podocyte excretion: Highly sensitive and specific marker (Garovic et al).

6. Enzymes and Hormones: Increased levels of plasma cystyl amino peptidase, Pappa-

A (Wood and Durham) and high level of β HCG (Noguera et al).

7. FOETAL DNA

Foetal DNA in maternal serum may be predictive of pre eclampsia.

PREVENTION OF PRE-ECLAMPSIA

Pregnancy is a process of physiologic adaptation which occur primarily is an effort to supply the developing fetus with their nutrients that are essential for its proper development and growth. Preventive measures have been concentrated to relieve vasospasm and to correct the disturbed prostaglandin synthesis which lead to platelet aggregation and endothelial damage. There are no definite preventive methods but attempt should be made for early detection of high risk patients. ***Thomas Brewer*** rightly stated that pre-eclampsia is a complication of maternal malnutrition whose symptoms can be largely eliminated by eating a well balanced diet.
A study by the ***Dietary Approaches to stop Hypertension (Dash)*** demonstrated that dietary manipulation significantly lowers the Blood pressure.
Prevention can dealt with

1. Non medical measures
2. Medical measures.

SALT RESTRICTION

This may be used as a means to prevent the onset of essential hypertension but not be used for gestational Hypertension and Pre-eclampsia.

BED REST

This may be useful in known hypertensive patients to reduce the severity.

FISH OIL

The benefit from fish oils seems to be associated with long chain n-3 fatty acids, C-20, n3 eicosepentoicacid and docosepentanoicacid & docosahexanoid acids. They decrease platelet aggregation on endothelial cells and leads a relative state of vasodilatation.

PLANT OIL

Linoleic and Evening primrose oil (3mg Linoleic + 32mg of Gammalinoleic acid / day.

CALCIUM

Proposed mechanism where by calcium supplementation may reduce blood pressure.

Reduced serum calcium

↓

Increases Vit. D stimulation - interact with renin / angisotensin

↓

(Through its link to PTH) Vit. D receptors present in the smooth muscle reduction of altered Vit. D metabolism smooth muscle proliferation

↓

Development of atherosclerosis

↓

Hypertension

High intake of calcium of 1.3g/d showed a reduced incidence of both Pre-eclampsia & Eclampsia (Villar, J American J Clin - Nutrition 1980). World Health Organization (2006) supplementation with calcium 1.5g/day significantly reduces the risk of maternal neonatal morbidity and preterm delivery in the later among young women.
Cochrane systematic review noted protective effects of calcium supplementation only in women with low calcium intake.

ANTIOXIDANT

Antioxidant therapy significantly reduced endothelial cell activation in a study performed by (Chappell and associates, Lancet 1999). There was a significant reduction in the incidence of Pre-eclampsia in women who was given with vitamin C and E.

MEDICAL MEASURES

Low dose aspirin appears to be beneficial for women at high risk of pre-eclampsia (Cochrane Review - 19% reduction in risk of pre-eclampsia).

AIM OF THE STUDY

To determine whether a low urinary calcium / creatinine ratio (≤ 0.04) in a spot urine sample, obtained in asymptomatic pregnant women between 24-34 weeks of gestation can predict the subsequent development of pre-eclampsia.

MATERIALS AND METHODS

This study was conducted at department of Obstetrics and Gynaecology, Govt. R.S.R.M.Lying in Hospital attached to Stanley Medical College, Royapuram, Chennai.
STUDY PERIOD: The Period of Study was from July 2008 – September 2009

STUDY DESIGN: PROSPECTIVE STUDY

150 Pregnant women were attending the antenatal clinic at R.S.R.M. Lying in Hospital, were registered in this study. Only those pregnant women whom we could follow to term and were planning delivery at R.S.R.M. Lying in Hospital, Royapuram Chennai, were included in this study.
150 normal pregnant women between 24 to 34 weeks of gestation were divided into two groups (1) study group comprised of 100 pregnant women with nulliparity (majority) as high risk factor for development of pre-eclampsia who were normotensive at registration with blood pressure <140/90 mmHg and no proteinuria on dipstick (2) control groups comprised of 50 normal multiparous women. With no risk factor what so ever for the development of pre-eclampsia were included.

PATIENTS SELECTION CRITERIA

Inclusion Criteria

1. Gestational age between 24-34 weeks.
2. Women who intented to have their deliveries at RSRM lying in hospital.

Exclusion Criteria

1. History chronic hypertension
2. History of Diabetes Mellitus
3. History of Renal disease
4. Blood pressure ≥ 140/90 mm Hg
5. Evidence of proteinuria by the dipstick method.

The study was done on asymptomatic primi, and pregnant women with Rh Negative, with previous h/o pre-eclampsia, family h/o
pre-eclampsia were also included.
2^{nd} and 3^{rd} gravida with no risk factors for development of
pre-eclampsia, were included in control group.

METHODOLOGY

In all the pregnant women included in the study, a written informed consent was obtained.

1. No dietary alterations were recommended
2. Detailed history was taken.
3. Complete examination
   i. General examination
   ii. Clinical examination
      – Cardiovascular system
      – Respiratory system
      – Central nervous system

   iii. Obstetric examination was done.

4. Blood Pressure
   i. In sitting posture
   ii. Phase Korotkoff V sound was taken to determine the diastolic component
5. Basic Investigations
   i. Haemoglobin
   ii. Blood Grouping and Rh Typing
   iii. Urine – Albumin
      – Sugar
      – Deposits
6. Single voided urine sample in the morning was collected from all the patients in calcium free vial and about 5ml of non-heparinized blood was collected at the same time.

   Both the urine and blood sample were sent to the Biochemistry Laboratory of Stanley Medical College hospital without delay.

7. Serum and urinary calcium estimation wad done using commercially available kits using, Ortho-cresolphthalein Complexone Method (OCPC) on a semi auto analyser.
8. Serum and urinary creatinine estimation was done by MODIFIED JAFFE'S METHOD on a semi auto analyser.
9. Followed up with routine antenatal visits for signs and symptoms of pre-eclampsia by routine examination of blood pressure, serial weight, edema, and investigation of pre-eclampsia when required and results were tabulated.
10. Mode of delivery and fetal outcome was noted

METHODS

Ortho-cresolphthalein complexone Method of estimation of Calcium.

PRINCIPLE

Calcium in alkaline medium combines with the O-cresolphthalein complexone to forms a purple coloured complex. Intensity of colour formed is directly proportional to the calcium concentration in the sample.

Ortho- cresolphthalein complexone reacts with calcium at pH 10.0 to form a purple coloured complex.

Calcium + OCPC → purple colour complex.

PROCEDURE:

500µl of reagent mixed with 10µl of samples incubated for 5 minutes at room temperature (25-30^{o}C). Absorbance of standard and sample is read against reagent blank at 578 nm with yellow filter with in 30 minutes.

TEST RESULTS

$$\textit{Calcium concentration in mg/dl} = \frac{\textit{Absorbance of test}}{\textit{Absorbance of Standard}} \times 10$$

CREATININE ESTIMATION BY MODIFIED JAFFE'S METHOD

Creatinine is the carbolic product of creatinine phosphate and it is excreted entirely by the kidneys. Creatinine reacts with picric acid, in alkaline medium to give orange coloured complex – creatinine Picrate (Jaffe's reaction). Intensity of colour formed during the fixed time is directly proportional to the amount of creatinine present in the sample.
Creatinine + Alkaline picrate → Orange coloured complex

Procedure:

Serum Creatinine

500µl of reagent and 50µl of sample added and mixed well and immediately reading was taken by using semi autoanalyser and estimate the colour at 520nm green filter.

Urinary Creatinine

500µl of reagent and 50µl of urine sample added after diluted in distilled water in one in 10 dilution mixed well and estimate the colour at 520nm using green filter. The urinary creatinine results was multiplied by 10.

RESULTS

TABLE – I:

DISTRIBUTION OF PERSONS IN STUDY AND CONTROL GROUP ACCORDING TO AGE

Age in years	*Study group*		*Control*		*Total*
	Number	*%*	*Number*	*%*	
17-22	64	64%	15	30%	52.7%
23-28	30	30%	26	52%	37.3%
29-34	6	6%	7	14%	8.7%
35-39	–	–	2	4%	1.3%
Total	100	100%	50%	100%	100%

Above table, shows the distribution of persons in study and control group according to age 52.7% in age group of 17-22, 37.3% in age group of 23-28, 8.7% in age group of 29-34 and 1.3% in age group 35-39%.

TABLE – II:

DISTRIBUTION OF PATIENTS WITH PRE-ECLAMPSIA ACCORDING TO AGE

Age in years	*Study group*		*Control group*	
	Total No.	*Pre eclampsia positive*	*Total No.*	*PE positive*

17-22	64	11	15	-
23-28	30	1	26	-
29-34	6	2	7	2
35-39	-	-	2	-
Total	**100**	**14**	**50**	**2**

According to **MacGillivary (1958)** the relationship of maternal age and incidence of pre-eclampsia gives a “J” shaped curve with high incidence among young primi gravida and markedly increased incidence among older primigravida. In study group preedampsia was high between 17-22 years and pre-eclampsia was high above 30 years.

TABLE – III:
DISTRIBUTION OF PATIENTS WITH PRE-ECLAMPSIA ACCORDING TO PARITY

PARITY	TOTAL	PRE-ECLAMPSIA POSITIVE	%
Nulliparous	94	12 (12.77%)	75%
Multiparous	56	4 (7.14%)	25%

Above table shows the distribution of patients with pre-eclampsia according to parity. Pre eclampsia is more common in nulliparous women. This table show high incidence of pre-eclampsia in nulliparous (75%) than in multiparous women, P value < 0.001 which is highly significant.

TABLE – IV:
INCIDENCE OF PRE-ECLAMPSIA IN RELATION TO PARITY IN STUDY & CONTROL GROUP

PARITY	STUDY GROUP					CONTROL GROUP				
	Total No.	Developed PE	Not Developed PE	Incidence		Total No.	Developed PE	Not Developed PE	Incidence	
				incidence	Over all incidence				incidence	Over all incidence
NULLIPAROUS	94	12 (85.71%)	82 (95.35%)	12.76%	14%	-	-	-	-	4%
MULTIPAROUS	6	2 (14.29%)	4 (4.65)	33.33%		50	2 (4%)	48 (96%)	4%	

The above table shows development of pre-eclampsia in relation to parity both in study group & control group. In study group the incidence was high (14) when compared to control group 4%.

TABLE – V:

RELATIONSHIP OF URINARY CALCIUM/ CREATININE RATIO AND DEVELOPMENT OF PRE-ECLAMPSIA

GROUP	DEVELOPED PRE-ECLAMPSIA		NOT DEVELOPED PRE-ECLAMPSIA		TOTAL
	NO	%	NO	%	

UCCR < 0.04 n = 16	13	81.25%	3	18.75%	16
UCCR > 0.04 n = 134	3	2.23%	131	97.76%	134
Total	**16**		**134**		**150**

This table shows the relationship of urinary calcium / creatinine ratio and development of pre-eclampsia in both study and control group.
16 patients showed urinary calcium creatinine ratio < 0.04 134 patients shows UCCR > 0.04. 81.25% of persons with UCCR < 0.04 and develop pre-eclampsia. 97.76% of persons with calcium / creatinine ratio > 0.04 doesn't develop pre-eclampsia P value <0.001 which is highly significant.

TABLE – VI:

RELATIONSHIP OF UCCR AND DEVELOPMENT OF PRE-ECLAMPSIA IN STUDY GROUP

Appearance of PE	UCCR < 0.04 (N=14)		UCCR > 0.04 (N=86)	
	No	%	No	%
Positive for PE	12	85.71%	2	2.33%
Negative for PE	2	14.29%	84	97.67%

This table shows development of pre-eclampsia in study group in relation to the cut off value of UCCR <0.04. Out of 100 patients 14 patients showed UCCR <0.04. Out of 14 patients 12 (85.71%) patients developed PE. 2 (14.9%) patients didn't develop pre-eclampsia with UCCR < 0.04. The remaining 86 patients showed a UCCR value of
> 0.04, in this group 2 patients developed pre-eclampsia (2.33%) 84 patients didn't develop pre-eclampsia (97.67%).

TABLE – VII:

RELATIONSHIP OF URINARY CALCIUM & CREATININE RATIO AND DEVELOPMENT OF PRE-ECLAMPSIA IN CONTROL GROUP

APPEARANCE OF PRE-ECLAMPSIA	UCCR < 0.04 n=2		UCCR > 0.04 n=48	
	NO.	%	No	%
Developed PE	1	50%	1	2.08%
Did not develop PE	1	50%	47	97.92%

Above table shows relationship of UCCR & development of pre-eclampsia in control group. 50% of person with UCCR < 0.04 developed pre-eclampsia and 50% didn't develop pre-eclampsia even with UCCR < 0.04. The remaining 48 pregnant women showed UCCR value of > 0.04, in this group one patient developed pre-eclampsia (2.08%), 47 patients did not develop pre-eclampsia (97.92%).

TABLE – VIII:

RELATIONSHIP OF SERUM CALCIUM (mg/dl) AND PRE-ECLAMPSIA

Serum Calcium (mg/dl)	Pre-eclampsia		Total
	Developed	Not developed	
<=7.5	14 (87.5%)	15(11.2%)	29 (19.3%)
7.6-8.5	2(12.5%)	72(53.7%)	74 (49.3%)
8.6-9.5	-	27(20.1%)	27 (18.0%)
9.6-10.5	-	13(9.7%)	13 (8.7%)
>10.5	-	7(5.2%)	7 (4.7%)
Total	**16**	**134**	**150 (100%)**

The above table shows 87.5% of those who developed pre-eclampsia had serum calcium level below 7.5 mg/dl and 12.5% who developed pre-eclampsia between 7.6 –8.5 mg/dl.
Chi square test P value <0.001 which is highly significant.

TABLE – IX:

DISTRIBUTION OF PATIENTS WITH PRE-ECLAMPSIA ACCORDING TO SERUM CREATININE

SERUM CREATININE mg /dl	PRE-ECLAMPSIA		**Total**
	DEVELOPED	NOT DEVELOPED	
0.6 – 0.7	-	89(66.4%)	89
0.8-0.9	10 (62.5%)	41 (30.6%)	51
1.0-1.2	6 (37.5%)	3 (2.2%)	9
>1.2	-	1 (0.74%)	1
Total	**16**	**134**	**150 (100%)**

This table shows development of pre-eclampsia in relation to serum creatinine. 62.5% patient developed pre-eclampsia in the range of 0.8 – 0.9% and 37.5% in range of 1.0 –1.2 mg/dl.

TABLE – X:
DISTRIBUTION OF PATIENT ACCORDING TO THEIR FIRST APPEARANCE OF PRE ECLAMPSIA IN WEEKS

Gestational age in weeks	Number of Patients
26-28	-
29-31	-
32-34	2
35-37	5
38-40	9
>40	-

The above table shows most patients developed pre-eclampsia between gestational age of 36 to 40 weeks indicating that the incidence is higher in later part of gestation.

TABLE – XI:
DISTRIBUTION OF PATIENTS ACCORDING TO SEVERITY OF PRE-ECLAMPSIA IN STUDY AND CONTROL GROUP

Type of pre-eclampsia	Study group	Control group
Mild Pre-eclampsia	13	2
Severe Pre-eclampsia	1	-
	14	2

The above table denotes that distribution of persons in study and control group according to severity of pre-eclampsia. 13 patients in the study group and two patients in the control group had mild pre-eclampsia and one patient in the study group had severe pre-eclampsia.

TABLE – XII:

PREDICTIVE VALUE OF URINARY CALCIUM / CREATININE RATIO AS A SCREENING TEST FOR PRE-ECLAMPSIA

Screening Test UCCR <0.04	***Developed pre-eclampsia***	***Not Developed pre-eclampsia***
Positive 16	13 (81.25%)	3 (18.75%)

Negative 134	3 (2.23%)	131 (97.76%)

13 out of 16 patients who developed pre-eclampsia had UCCR < 0.04

Using Chi square tests

P value <0.001 which is highly significant.

This screening test has

- Sensitivity of 81%
- Specificity of 98%
- Positive predictive value of 81%
- Negative predictive value of 98%

DISCUSSION

Though by definition, pre-eclampsia can occur at any time after
20 weeks of gestation it usually develops at the end of pregnancy, during labour (or) in immediate post partum period.
Renal function changes in pre-eclampsia have been documented and several prospective studies indicate that atleast some of these changes are present before the diagnosis of pre-eclampsia.

The present study was conducted on asymptomatic pregnant women between 24-34 weeks of gestation. All the women included in the study were normotensive with a blood pressure <140/90 mmHg, did not have pedal odema, and no proteinuria by dipstick method. In study group majority (96%) of the patients were nulliparous. Nulliparity as a risk factor was chosen because of very high incidence of pre eclampsia in nulliparity. 15 times greater risk compare to multiparity. In control group exclusion criteria was used and patients were picked up.

The morning urine sample was collected in calcium free vials and anlaysed for calcium and creatinine levels. Spot urine calcium and creatinine ratio was taken in this study because it correlated well with 24 hours calcium excretion. At the same time serum calcium and creatinine level were also estimated to see if there was any correlation.

In this study 150 patients were registered and 50 in the control group. Out of 150 patients 16 developed pre-eclampsia with incidence of 10.66% who was diagnosed with high blood pressure and proteinuria with (or) with out odema.

INCIDENCE

Mudaliar & Menon	10%
Sanchez Ramos	14%
Ritu Kamara et al	13.6%
Rodriguesz et al	10.6%
Present study	10.7%

Present study shows 10.7% incidence of pre-eclampsia which is similar to Rodriguez et al and Mudaliar Menon study.

AGE INCIDENCE

Women of different age group were included in the study and control group. 68.75% of those who developed pre-eclampsia were in the age group of between 17-22 years. This is accordance with **MACGILLVIRAY'S** report on age incidence of Pre-eclampsia which states that the incidence of pre-eclampsia is high among young primigravida. 12.5% of those who developed pre-eclampsia were in the age group more than 30 yrs.

Observation showed that the extremes of age group has prediliction for pre-eclampsia.

In control group comprising of multiparous women, in this group, pre-eclampsia developed in later age group because they might have an latent underlying hypertension.

PARITY

The incidence of pre-eclampsia is high in nulliparous that is 75% when compare to multiparous women (25%)

Those who developed pre-eclampsia in study group among nulliparity 12.76% and multiparity in both in study and control group was 7.14%

The over all incidence of pre-eclampsia in this study 10.66%. The over all incidence of pre-eclampsia in nulliparous women in this study 8%.

The incidence of pre-eclampsia in primigravida quoted in different studies.

Long & Oats	14.1%
Norwitz et al.,	11.9%
Williams	7.6%
Present study	8%

Our study showed results similar to the study by Williams.

The overall incidence of pre-eclampsia in multiparity 2.6%. he incidence of pre-eclampsia in multigravida quoted in different studies.

Study	**%**
Norwitz et al.,	4.6%

Long & Oats	5.7%
Study by Campell	0.8 – 2.6%
Present study	2.6%

Our study similar to Campell study.

Since most of the patients in RSRM –lying in hospital belonging only to low socio-economic status. So comparison could not be done between different socio economic groups in this study.

The value of urinary calcium and creatinine ratio <0.04 taken as the cut-off value for prediction of pre-eclampsia.

16 pregnant women out of 150 pregnant women had UCCR <0.04. Out of which 13 developed pre-eclampsia (81.25%) and remaining 3 did not develop pre-eclampsia (18.75%). Sensitivity being 81%, specificity being 98%, the positive predictive value of 81%, and the Negative predictive value of 98% and p value = <0.001 highly significant (using pearson chisquare table)

Analysis of results shows 81.25% of patients with UCCR <0.04 developed pre-eclampsia subsequently. 18.75% of patients with
UCCR <0.04 did not develop pre-eclampsia. Only 2.23% of patients with UCCR >0.04 developed pre-eclampsia subsequently, 97.76% of pregnant women with UCCR >0.04 did not develop pre-eclampsia subsequently.

Among study group 14 patients had UCCR <0.04 out of which 12 patients developed pre-eclampsia with an incidence of 85.71% and 2 out of 14 who had UCCR <0.04 did not develop pre-eclampsia with an incidence of 14.29%. 86 (86%) pregnant women showed UCCR >0.04 out of which 2 patients developed pre-eclampsia (2.33%) and 97.67% did not develop pre-eclampsia sensitivity being 85%, specificity 97% postive predictive value 85.7% and negative predictive value of 97.6% p<0.001 (chi square chart).

In control group, 2 patients had UCCR < 0.04 out of which one patient developed with an incidence of 50% and 1 out of 2 with UCCR<0.04, did not develop PE (50%). 48 pregnant women (96%) had UCCR>0.04 out of which one patient developed pre-eclampsia (2.08%) and where as 97.92% with UCCR >0.04 did not develop pre-eclampsia.

The mean urinary calcium in those who developed pre-eclampsia was 6.50 mg/dl. When it compared to 16.1mg/dl who did not develop pre-eclampsia. The difference was statistically significant (<0.001). This is an accordance with the hypocalciuria observed in pre-eclampsia by various workers **Taufield,**

Huikeshoven, Zwidershovdt & Suarez 1990.

The mean serum calcium was 6.9 mg/dl in patient with who developed pre-eclampsia when compared to 8.5mg/dl in pre-eclampsia negative group. P value < 0.001 which is highly significant.

In our study those who developed pre-eclampsia (87.5%) had serum calcium level below 7.5mg/dl and 12.5% had values between
7.6-8.5mg/dl and 12.5% had values between 7.6-8.5 mg/dl. None of the patients with greater serum calcium values developed pre-eclampsia. Calcium deficiency has been implicated as a predisposing factor for the development of pre-eclampsia- BELIZAN, SANCHEZ, RAMOS 1991. Calcium supplementation reduces the occurrence of pre-eclampsia.

The mean serum creatinine in those who developed pre-eclampsia was 0.96 mg/dl while it was 0.71 mg/dl in those who did not develop pre-eclampsia. Our study shows those who developed pre-eclampsia (62.5%) had serum creatinine value between 0.8-0.9mg/dl and 37.5% shows the value between 1-1.2 mg/dl.

When family history of pre-eclampsia was taken into account
2 cases was having family history of pre-eclampsia only one case showed UCCR <0.04 and that patient developed pre-eclampsia (100%).

One only patient had history of pre-eclampsia in previous pregnancy and the same patient had UCCR <0.04 and developed pre-eclampsia at gestational age of 36 weeks (100%).

The following table shows the percentage of patients with UCCR <0.04 by different authors in their study.

Rodriguez et al.,	UCCR <0.04	83.0%
Suzuki et al., 1992	UCCR <0.04	58.0%
Kamra et al., 1997	UCCR <0.04	71.4%
Present study	UCCR <0.04	81.5%

Our study is similar to Rodriguez et al., study.

2 patients in the study group and one patient (2.08%) in the control group with UCCR >0.04 developed pre-eclampsia.

From this study it has been found that most of the persons with the UCCR < 0.04 developed pre-eclampsia between gestational age of 36-40 weeks indicating that the incidence is higher in later part of

gestation.

This study shows that low UCCR in nulliparous is a very strong risk factor in development of pre-eclampsia in late pregnancy.

Comparison of predictive value of UCCR in present study with other studies

Author	*Year*	*No of patients*	*Parity*	*Sensitivity in %*	*Specificity in %*	*PPV in %*	*NPV in %*
Rodriguez et al	1988	88	>0	70	95	64	96
Sanches Ramos et al	1991	99	0	88	84	32	99
Ozcan et al	1995	56	0	63	96	71	93
Ritu Kamra et al	1997	104	>0	71.4	95.38	64.23	96.51
Kar Srivastava	1999	100	>0	75	94.38	64.23	96.51
Present Study	2009	150	>0	81	98	81	98

COMPARISON OF OUR STUDY WITH OTHER STUDY

In our study with low UCCR (<0.04) 81.25% developed pre-eclampsia which is similar to Rodrigruez et al.

Karsrivastava study shows negative predictive value of 96.5% our study showed negative predictive value of 98%.

Positive predictive value was highest in our study (81%) and in the Ozcan et al study shows 71%.

Maximum specificity was shown by Ozcan et al., 1995 of 96% and our study noted with 98% of

values.

Sanchez Ramos et al., in his study of 99 patients shows a very high sensitivity of 88% and our study shows 81%. As per Sanchez Ramos et al., study (Obstet gynecol 1991 April 77 (4): 510-3) sensitivity of 85% specificity of 91% and positive predictive value and negative predictive value of 85%, 91% respectively. Our study well correlated with Sanchez Ramos et al., study.

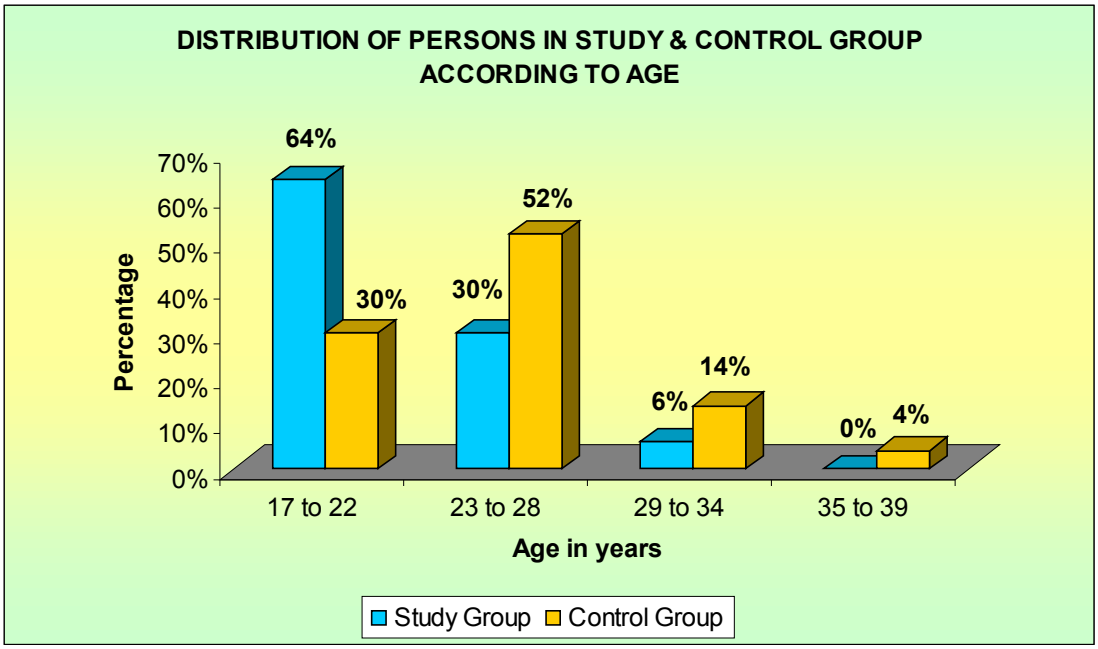
Izumi & Minakami (1997) measured calcium and creatinine concentration in spot urine samples at 12 weeks (or) less of gestation. But they concluded that determination of calcium / creatinine ratio in spot urine sample in the 1st trimester is of only limited clinical value for identifying the patients with an increased risk for pre-eclampsia

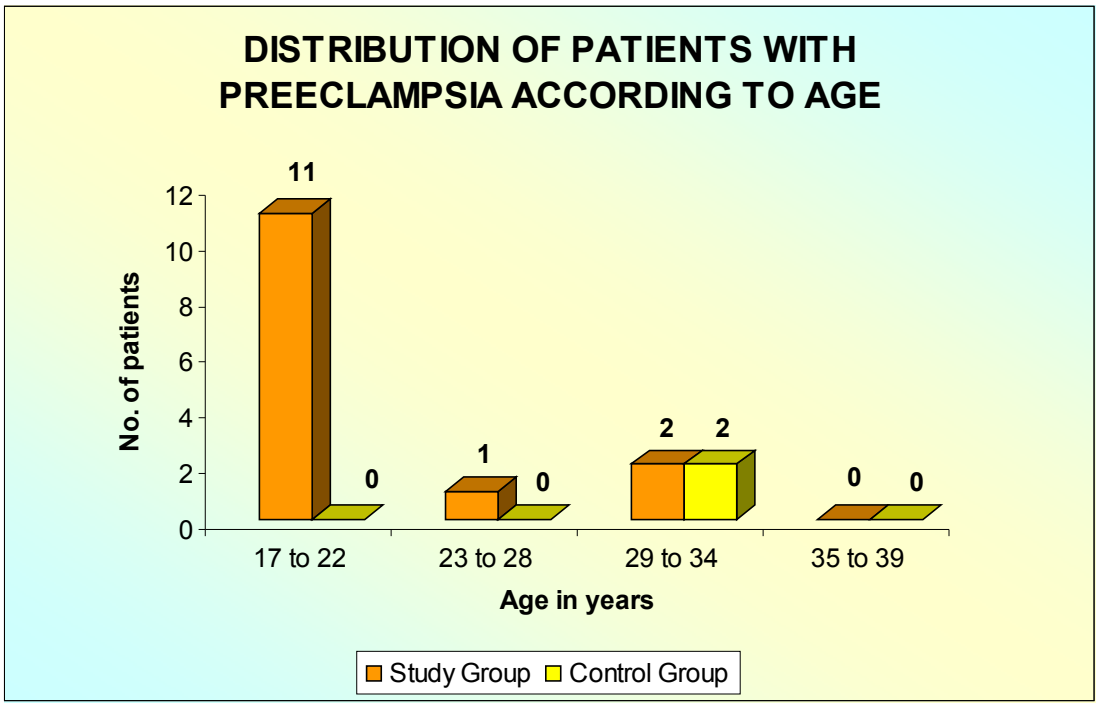
Thus determination of UCCR in spot urine sample is valuable in predicting subseqeunt development of pre-eclampsia when a value of <0.04 is taken as cut off. (Kazerooni et al 2003 (< 0.03).

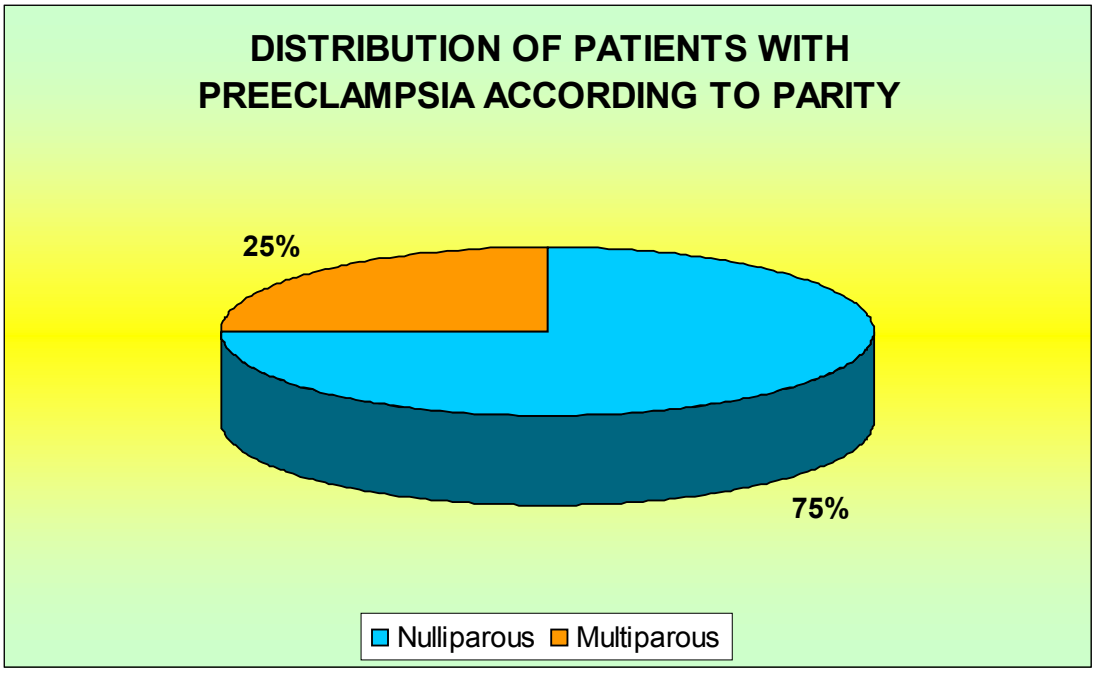
On statistical analysis, it was found that when UCCR is taken as a predictor of pre-eclampsia it was highly significant.

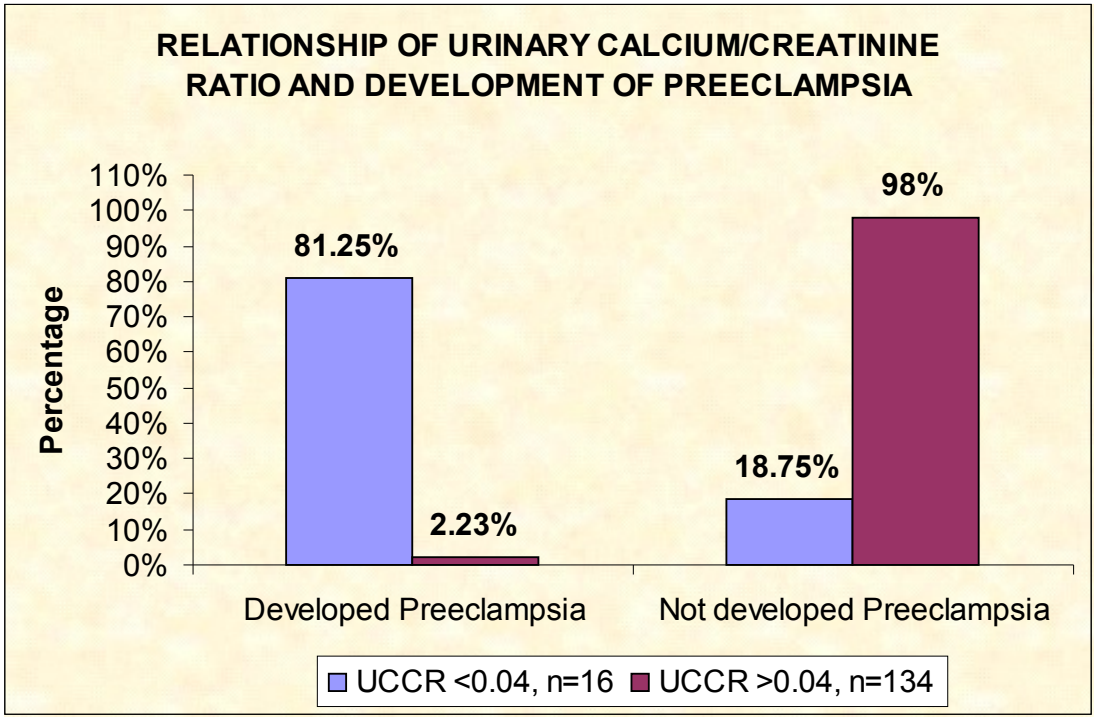
By using chi square test p value of <0.001 was arrived at which is highly significant.

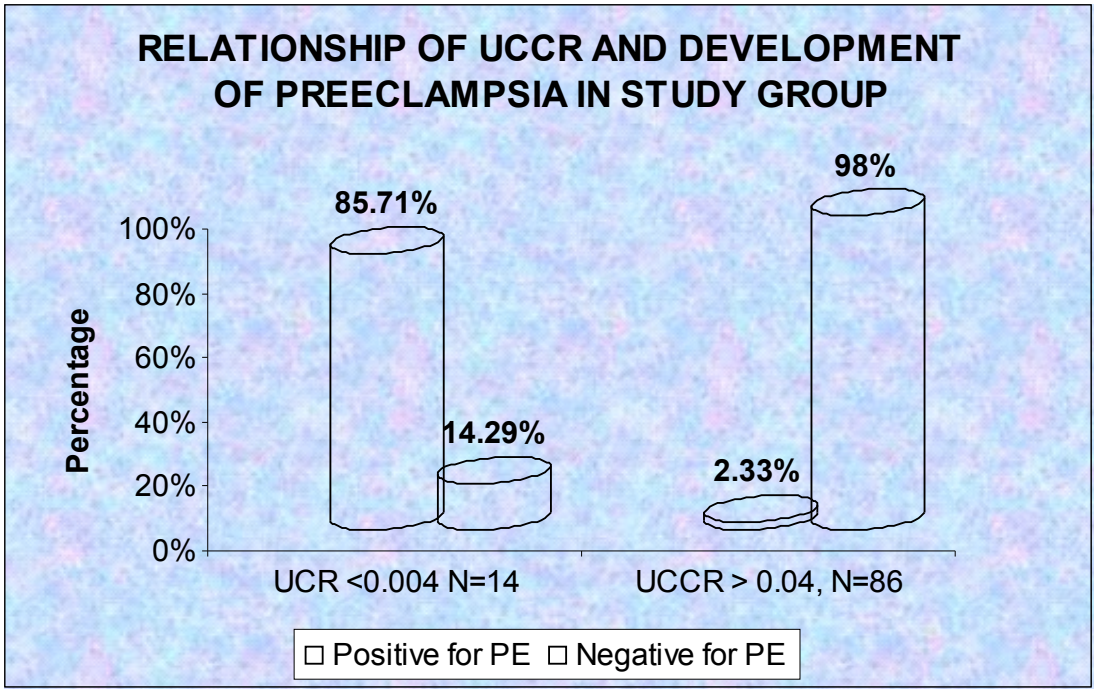
The **OCPC method** of estimation of urinary calcium and **modified Jaffe's method** of creatinine measurement is more accurate due to consistent way of estimation. Hence the results are accurate proving the worth of the test.

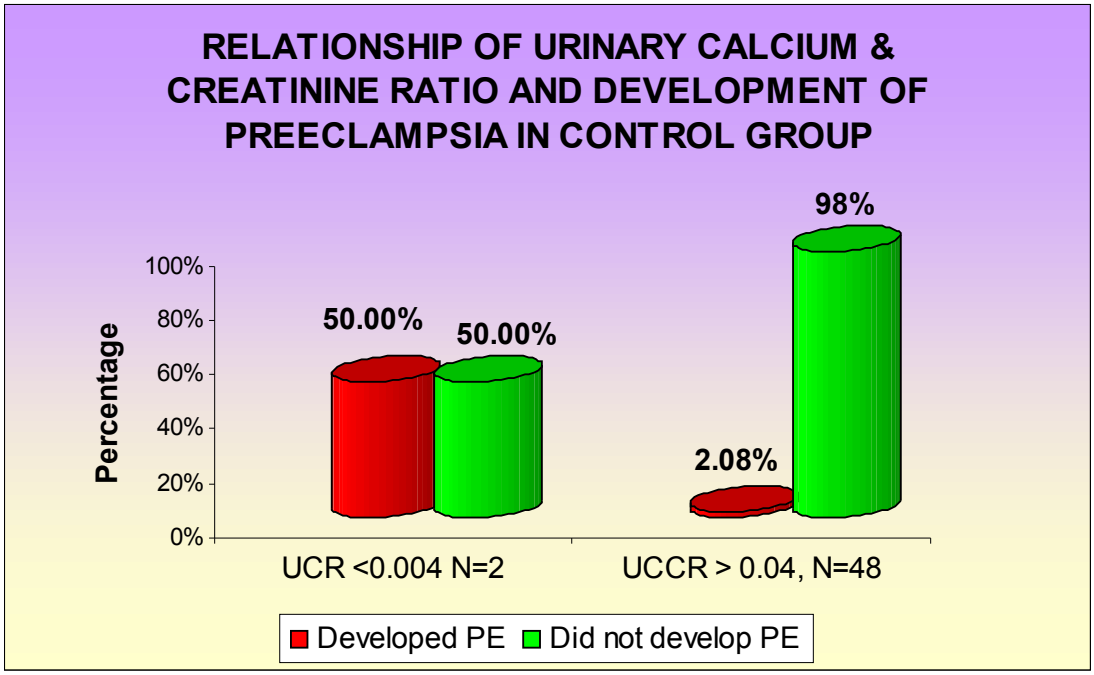

DISTRIBUTION OF PERSONS IN STUDY & CONTROL GROUP ACCORDING TO AGE
Percentage
70%
60%
50%
40%
30%
20%
10%
0%
64%
30%
30%
52%
6%
14%
0%
4%
17 to 22
23 to 28
29 to 34
35 to 39
Age in years
Study Group
Control Group

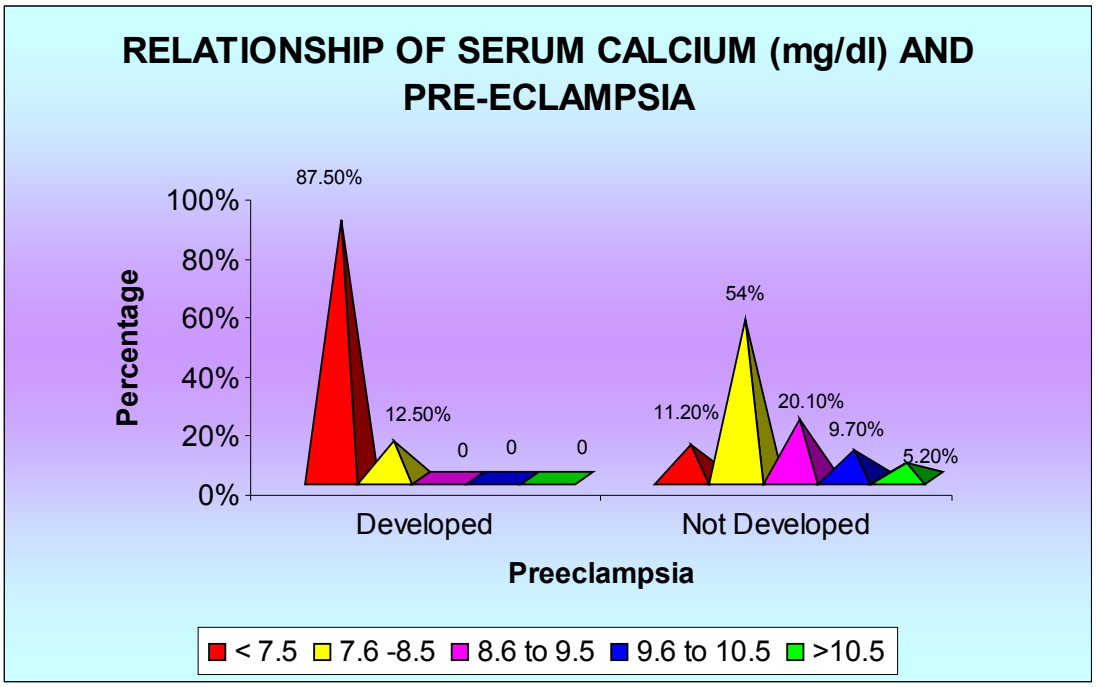

DISTRIBUTION OF PATIENTS WITH PREECLAMPSIA ACCORDING TO AGE
No. of patients
12
10
8
6
4
2
0
11
0
1
0
2
2
0
0
17 to 22
23 to 28
29 to 34
35 to 39
Age in years
Study Group
Control Group

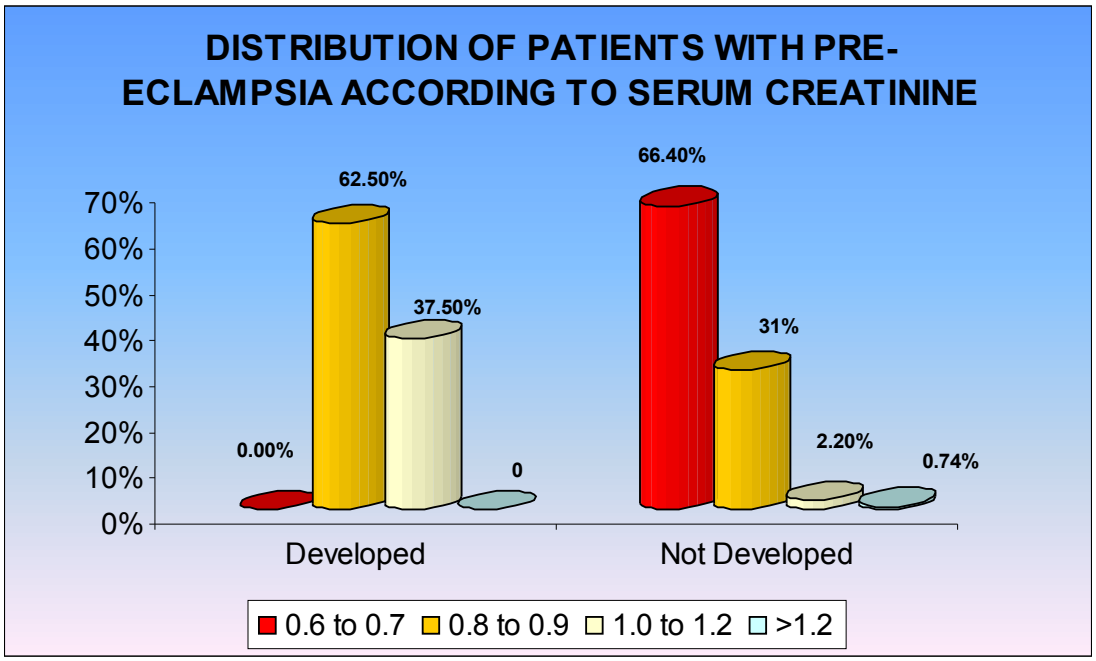

DISTRIBUTION OF PATIENTS WITH PREECLAMPSIA ACCORDING TO PARITY
25%
75%
Nulliparous
Multiparous

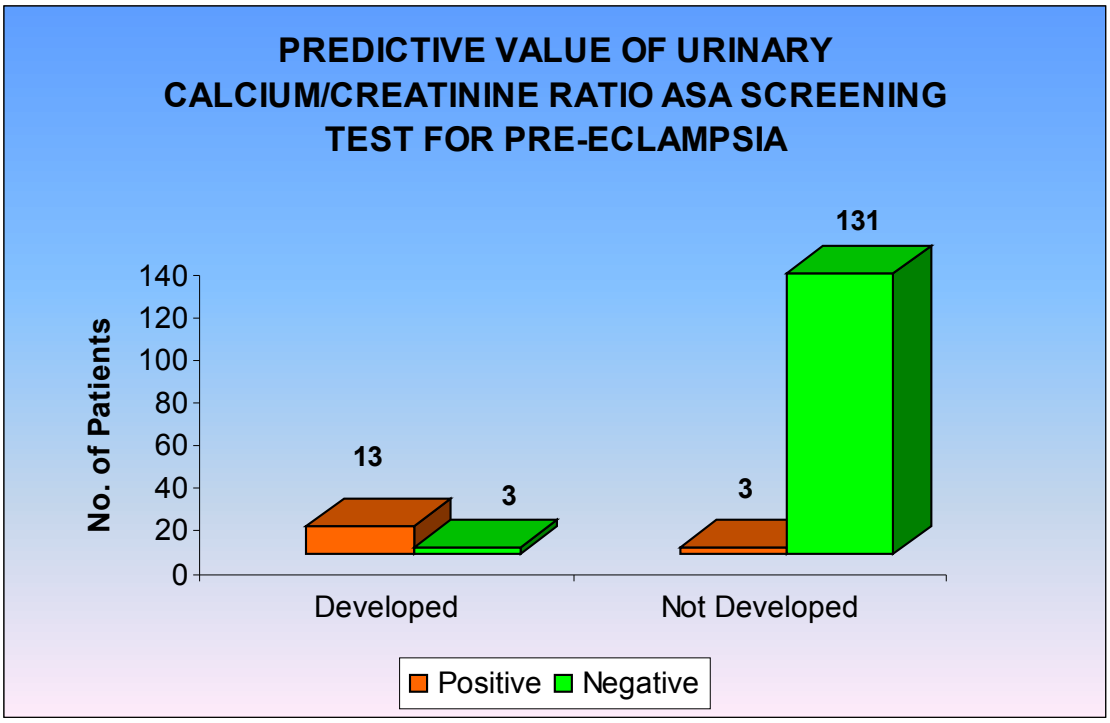

RELATIONSHIP OF URINARY CALCIUM/CREATININE RATIO AND DEVELOPMENT OF PREECLAMPSIA
Percentage
110%
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
81.25%
2.23%
18.75%
98%
Developed Preeclampsia
Not developed Preeclampsia
UCCR <0.04, n=16
UCCR >0.04, n=134

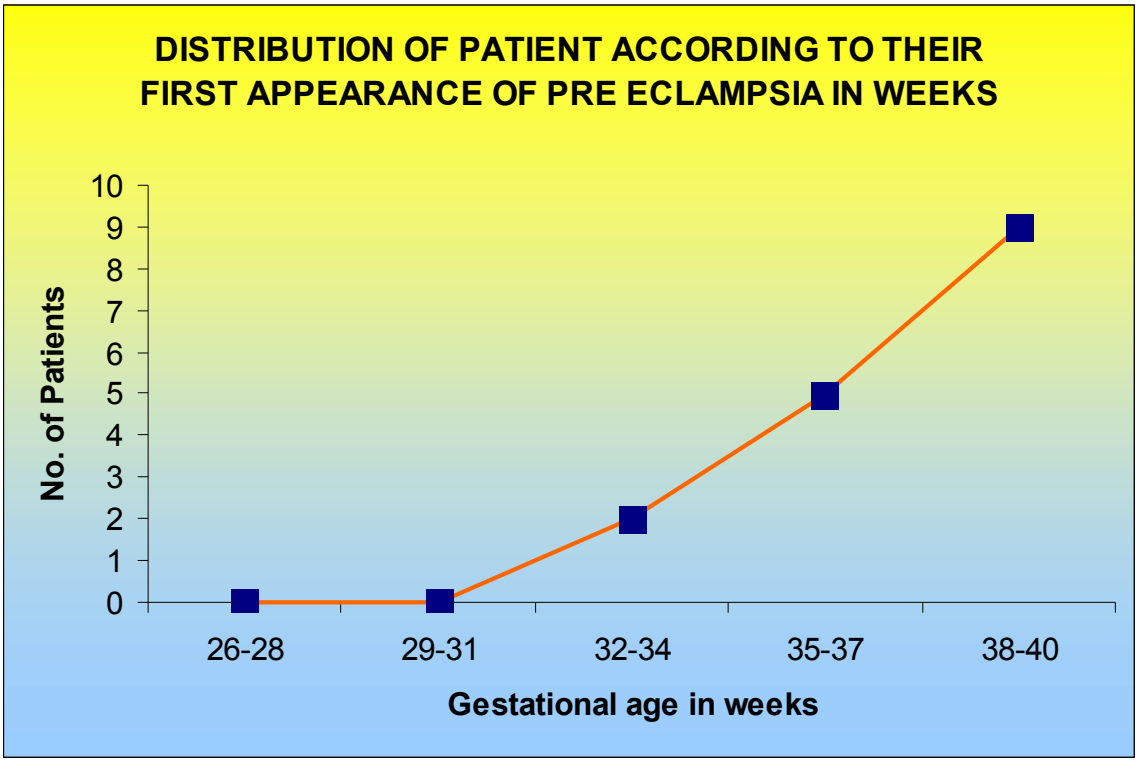

RELATIONSHIP OF UCCR AND DEVELOPMENT OF PREECLAMPSIA IN STUDY GROUP
Percentage
100%
80%
60%
40%
20%
0%
85.71%
14.29%
2.33%
98%
UCR <0.004 N=14
UCCR > 0.04, N=86
Positive for PE
Negative for PE

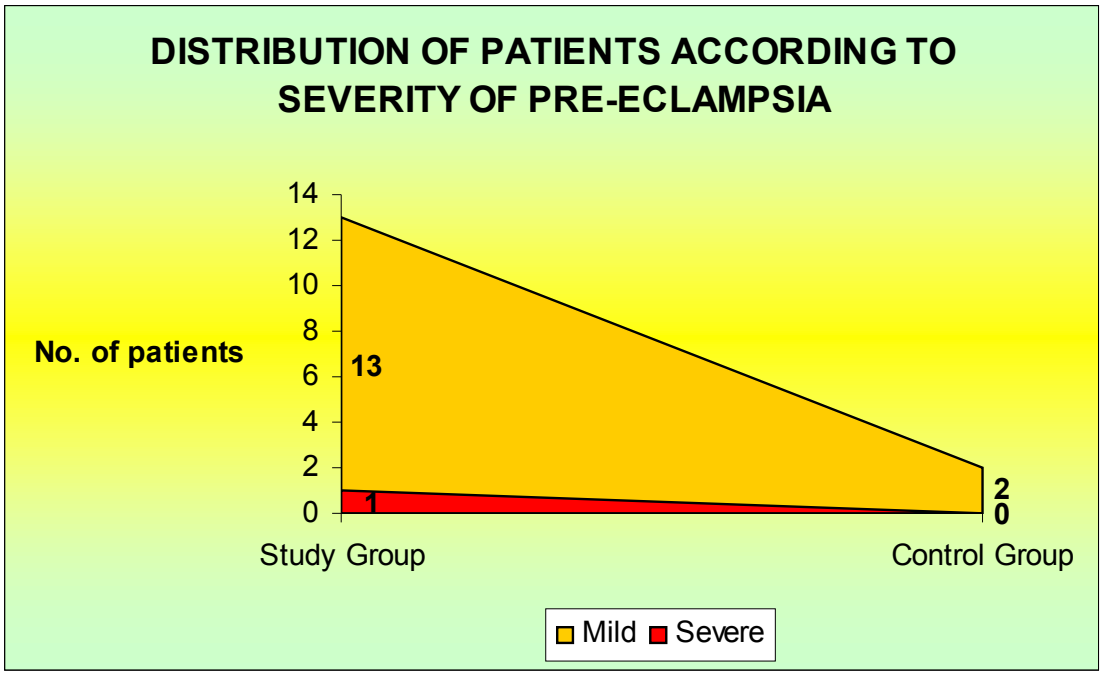

RELATIONSHIP OF URINARY CALCIUM & CREATININE RATIO AND DEVELOPMENT OF PREECLAMPSIA IN CONTROL GROUP
Percentage
100%
80%
60%
40%
20%
0%
50.00%
50.00%
2.08%
98%
UCR <0.004 N=2
UCCR > 0.04, N=48
Developed PE
Did not develop PE


RELATIONSHIP OF SERUM CALCIUM (mg/dl) AND PRE-ECLAMPSIA
Percentage
100%
80%
60%
40%
20%
0%
87.50%
12.50%
0
0
0
54%
11.20%
20.10%
9.70%
5.20%
Developed
Not Developed
Preeclampsia
< 7.5
7.6 -8.5
8.6 to 9.5
9.6 to 10.5
>10.5


DISTRIBUTION OF PATIENTS WITH PRE-ECLAMPSIA ACCORDING TO SERUM CREATININE
70%
60%
50%
40%
30%
20%
10%
0%
0.00%
62.50%
37.50%
0
66.40%
31%
2.20%
0.74%
Developed
Not Developed
0.6 to 0.7
0.8 to 0.9
1.0 to 1.2
>1.2


PREDICTIVE VALUE OF URINARY CALCIUM/CREATININE RATIO ASA SCREENING TEST FOR PRE-ECLAMPSIA
No. of Patients
140
120
100
80
60
40
20
0
13
3
3
131
Developed
Not Developed
Positive
Negative


DISTRIBUTION OF PATIENT ACCORDING TO THEIR FIRST APPEARANCE OF PRE ECLAMPSIA IN WEEKS
No. of Patients
10
9
8
7
6
5
4
3
2
1
0
26-28
29-31
32-34
35-37
38-40
Gestational age in weeks


DISTRIBUTION OF PATIENTS ACCORDING TO SEVERITY OF PRE-ECLAMPSIA
No. of patients
14
12
10
8
6
4
2
0
13
1
2
0
Study Group
Control Group
Mild
Severe

SUMMARY

The results of analysis of the study is summed up as follows:

1. Pre-eclampsia developed in 10.66% of tested patients population between 36-40 weeks of gestation mostly. Patients developed pre-eclampsia in the form of raised blood pressure, proteinuria and with or without odema.
2. Nulliparity was found to be a significant high risk factor.
3. Family history of pre-eclampsia and previous history pre-eclampsia also a high risk factor for development of pre-eclampsia in 2 cases.
4. Urinary Calcium Creatinine ratio was < 0.04 in 10.66% patient out of which 81.25% that is 13 patients developed pre-eclampsia which was found to be statistically highly significant with the p value of <0.001.
5. Serum calcium level also found to be low in patients who developed pre-eclampsia and serum creatinine level also found to be higher.
6. Sensitivity 81%, specificity 98% Positive predictive value 81% Negative predictive value of 98% P= <0.001 which is highly significant.

CONCLUSION

The study shows that spot urinary calcium creatinine ratio with the cut off value of < 0.04 done between 24-34 weeks of gestation is an excellent screening tool for the prediction of pre-eclampsia among numerous screening test with specificity of 98% and sensitivity of 81%, and positive predictive value 81%, and negative predictive value 98%.

A young nullipara along with low UCCR is especially at a high risk for development of pre-eclampsia.

This test is ideal because

- Simple and easy to perform
- In expensive
- Non invasive and convenient for the patient
  Low UCCR value helps in identify the population who is at greatest risk to be included in primary preventation program.

Hence in routine antenatal care with screening test like urinary calcium Creatinine ratio in spot urine sample with the cut off value of <0.04 can be applied as a screening test for all women then this dreadful multisystemic condition can be treated in time.

PROFORMA SHEET

NAME : AGE : IP NO : UNIT :
ADDRESS :

DISSERTATION REF No :

EDUCATIONAL STATUS :

SOCIO-ECONOMIC STATUS :

MENSTRUAL HISTORY : L.M.P
E.D.D.
CYCLES :

MARITAL HISTORY
OBSTETRIC INDEX
GRAVIDA : PARA : LIVE : ABORTION :
HISTORY :

PAST HISTORY : PIH / PRE ECLAMPSIA / RENAL DISEASE /

RECURRENT ABORTION

H/O MOTHER / SISTER / AUNT WITH H/O PRE ECLAMPSIA

FAMILY HISTORY : HYPERTENSION, EPILEPSY

DIABETES MELLITUS

RENAL DISEASE

OTHERS

MEDICAL HISTORY : HISTORY OF CHRONIC HYPERTENSION
DIABETES MELLITUS
RENAL DISEASE
HEART DISEASE
EPILEPSY

PERSONAL HISTORY: SMOKING/ ALCOHOL CONSUMPTION/ DRUG ABUSE

OBSTETRIC HISTORY

PREVIOUS – PREGNANCY – DETAILED HISTORY

PRESENT OBSTETRIC HISTORY :

I TRIMESTER -FEVER, DRUG, INTAKE, RADIATION, BLEEDING PV

II TRIMESTER – BLEEDING, PEDAL EDEMA, VOMITTING, HEADACHE,

VISUAL DISTURBANCES

III TRIMESTER – BLEEDING, PEDAL EDEMA, VOMITTING, HEADACHE,

VISUAL DISTURBANCES

GENERAL EXAMINATION:

- HEIGHT
- WEIGHT
- BUILT
- NOURISHMENT
- ANEMIA / JAUNDICE/LYMPHADENOPATHY
- PEDAL EDEMA
- THYROID
- BREAST
- C.V.S
- R.S.
- PULSE

BLOOD PRESSURE: LEFT LATERAL / SUPINE / SITTING

PER ABDOMEN

- TRIMESTER II / III
- CORRESPONDING TO PERIOD TO AMMENORRHOEA
- ABDOMINAL WALL EDEMA
- FOETAL PRESENTATION
- LIQOUR
- FETAL HEART RATE

INVESTIGATION:

- URINE – ALBUMIN
  - SUGAR
  - DEPOSITS
- URINE CALCIUM
- URINE CREATININE
- URINARY CALCIUM CREATININE RATIO
- HAEMOGLOBIN
- COMPLETE BLOOD COUNT
- BLOOD GROUPING AND Rh TYPING
- SERUM CALCIUM
- SERUM CREATININE
- BLOOD UREA

USG - ABDOMEN AND PELVIS

FOLLOW UP AT TERM BLOOD PRESSURE

PROTEINUREA EDEMA

DELIVERY - LABOUR NATURAL / FORCEPS / LSCS

BABY - MALE/FEMALE

WEIGHT

APGAR

POSTNATAL PERIOD

e	BP	Wt	Gastational Age	Odema legs	Urine Albumin	Serum calcium	Serum Creatinine	Urinary Calcium	Urinary Creatinine	Urinary calcium Creatinine ratio	Other Sign Symptoms Pre-ecmlap

ABBREVIATION

ABBREVIATIONS USED IN THIS DISSERTATION

ACOG	American College of Obstetrics and Gynaecology
ALT	Alanine Amino Transferase
AST	Aspartate Amino Transferase
BP	Blood Pressure
Fam.H/o PIH	Family History of PIH
hCG	Human Chorionic gonadotrophin
HT	Hypertension
OCPC	Ortho Cresolphthalein Complexone
PE	Pre-eclampsia
PIH	Pregnancy Induced Hypertension
Prev. PIH	Previous History of Pregnancy Induced Hypertension
Primi	Primigravida
PTH	Parathormone
p value	Probability value
UCCR	Urine calcium Creatinine ratio
WHO	World Health Organisation
H/o	History of
IL	Interleukin
TNF	Tumor Necrosis Factor
Vit. D	Vitamin D
CVS	Cardiovascular System
RS	Respiratory System

CNS	Central Nerve System
P/A	Per abdomen
USG	Ultrasonogram

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Semi Auto Analyser and calcium and creatinine kit used for the study

MASTER CHART

STUDY GROUP

S. No.	Name	Age	Obstetric Code	IP No.	Socio Economic Status	High Risk factors	Serum		Urinary		UCCR	
							Calcium	Creatinine	Calcium	Creatinine		
1.	Malathi	20	Primi	7132	V		7.4	0.6	10.5	162	0.064	
2.	Kasthuri	22	Primi	7240	IV		8.0	0.7	15.2	185	0.082	
3.	Devi	20	Primi	7237	V		8.4	0.8	14.5	191	0.075	
4	Kalpana	19	Primi	7254	IV		6.9	0.7	10.9	172	0.063	
5	Dhana Lakshmi	17	Primi	7224	V		7.3	0.9	12.4	182	0.068	
6	Lakshmi	20	Primi	7209	V		10.4	0.9	16	175	0.091	
7	Anjali	22	Primi	7245	IV		7.5	1.0	4.5	145	0.031	D e
8	Jaqulin	22	Primi	7233	IV		8.2	1	13.9	234	0.059	
9	Thenmozhi	19	Primi	7241	V		8	0.6	16.7	197	0.084	
10	Amulu	18	Primi	2176	IV		8	0.6	14.2	145	0.097	
11	Vasanthi	17	Primi	10421	V		8.4	0.9	14.9	216	0.068	
12	Tamilarasi	27	Primi	7202	V		7.7	0.7	13.9	200	0.069	
13	Mary	21	Primi	7261	IV		10.3	0.8	19.0	191	0.099	
14	Kathaleeswari	17	Primi	9787	V		9.8	0.6	17.1	199	0.085	
15	Priya	19	Primi	9532	IV		10.9	0.7	20.1	174	0.115	
16	Umamaheswari	22	Primi	7096	V		8.2	0.7	16.1	245	0.057	

17	Prema	21	Primi	7242	V		7.2	0.8	12	154	0.077	
18	Logeswari	18	Primi	9687	IV		8	0.9	13.6	240	0.056	
19	Velumayil	26	G2P1L1	10397	IV	Hypothyroidsm	8.5	0.7	16.7	231	0.072	
20	Nagajothi	19	Primi	9552	IV		7.4	1.2	6.9	188	0.036	D e
21	Selvi	24	Primi	7315	V		11.0	0.8	11.8	196	0.060	
22	Lakshmi	28	G2P1L1	1571	IV	Family H/O PE	10	0.7	18.1	189	0.095	
23	Premalatha	19	Primi	7564	V		6.8	0.9	5.8	160	0.036	D e
24	Saraswathy	24	Primi	7392	V		7.9	0.7	14.1	177	0.079	
25	Salsa	23	Primi	7164	V		8.4	0.8	15.1	213	0.070	

S. No.	Name	Age	Obstetric Code	IP No.	Socio Economic Status	High Risk factors	Serum		Urinary		U
							Calcium	Creatinine	Calcium	Creatinine	
26	Sridevi	20	Primi	7201	V		7.3	0.8	12.5	240	0
27	Vijayalakshmi	19	Primi	9625	V		7.2	0.8	11.2	182	0
28	Bharaathi	18	Primi	9782	V		7.6	0.9	14	142	0
29	Vijayalakshmi	23	G2P1L1	9769	V	Rh ---	9.2	0.7	17.1	199	0
30	Sharmila	21	Primi	10280	V		8.5	0.6	12	235	0
31	Charulatha	23	Primi	9781	V		8.5	0.6	16.8	250	0
32	Sunitha	22	Primi	1730	V		9.3	0.6	18.4	201	0
33	Kalaiselvi	23	Primi	1142	IV		9.6	0.8	15.7	211	0
34	Sudha	24	Primi	1203	IV		8.6	0.9	13.9	163	0
35	Vanitha	18	Primi	1196	IV		8.4	0.7	14.1	231	0
36	Nazeera	21	Primi	2187	IV		8.1	0.8	14.1	202	0
37	Meena	20	Primi	9595	IV		7.2	0.6	14.2	186	0
38	Mary	20	Primi	1875	V		7.2	0.6	12	186	0
39	Gajalakshmi	20	Primi	9500	V		7.6	0.6	12.4	202	0
40	Kalaivani	24	Primi	7579	V		7.7	0.6	13	214	0
41	Rani	28	G2P1L1	10127	IV	Family H/O PE	6.5	0.9	5.5	175	0
42	Vedavalli	22	Primi	7608	IV		6.8	1.1	5.2	153	0
43	Sudha	24	Primi	6219	IV		8	0.7	14.9	167	0
44	Sumathi	25	Primi	1301	IV		8.1	0.7	16	241	0
45	Shamsath	20	Primi	1131	IV		7.5	0.8	14.2	163	0
46	Dhanalaxmi	21	Primi	12268	IV		6.8	1.0	5.2	182	0
47	Arokyamay	21	Primi	1546	V		7.9	0.8	7.1	140	0
48	Sumathi	23	Primi	9729	V		8	0.7	15.3	210	0
49	Vijayalakshmi	23	Primi	2170	V		8.1	0.6	14.9	231	0
50	Malarkodi	20	Primi	1050	V		8	0.7	15.3	210	0

Name	Age	Obstetric Code	IP No.	Socio Economic Status	High Risk factors	Serum		Urinary		UCCR	Outcome	
						Calcium	Creatinine	Calcium	Creatinine			
jahan	20	Primi	1148	V		8	0.7	15.2	265	0.057		
swari	25	G2P1L1	1202	V	Rh ---	6.8	0.8	7.9	260	0.030		
athi	28	Primi	6067	V		8.4	0.9	16.8	250	0.067		
a	19	Primi	6442	V		8	0.8	16.3	292	0.057		
i	20	Primi	5412	V		7.6	0.7	11.4	180	0.063		
araiselvi	20	Primi	7278	V		6.5	1.0	5.7	210	0.028	Developed Pre-eclampsia	3
a	21	Primi	5139	V		8	0.7	15.5	200	0.075		
eswari	25	Primi	2222	V		8.2	0.6	15.7	214	0.073		
a	22	Primi	1617			7.9	0.9	13.9	201	0.067		
swari	18	Primi	7944			6.5	1.1	5.6	220	0.025	Developed Severe Pre-eclampsia	3
mala	20	Primi	4434	IV		8.1	0.8	16.4	206	0.079		
ya	20	Primi	7660	IV		8.3	0.8	15.1	235	0.064		
ya	25	Primi	1753	IV		7.9	0.7	13.5	192	0.070		
ani	19	Primi	2198	IV		9	0.7	16.2	218	0.074		
lakshmi	30	Primi	2177	IV		8.2	0.6	14.9	214	0.069		
ika	18	Primi	1171	IV		8.4	0.6	15	254	0.059		
thi	32	Primi	12285	IV		6.7	0.9	5.5	165	0.033	Developed Pre-eclampsia	3
nisha	28	Primi	1124	V		8.8	0.6	14.2	182	0.078		
ulakshmi	21	Primi	959	V		8.2	0.6	14.8	165	0.089		
thi	28	Primi	2183	V		9.1	0.7	17.1	209	0.081		
akala	20	Primi	9602	V		9.4	0.7	16.6	210	0.079		
a	22	Primi	972	V		8.5	0.7	16.2	298	0.081		
	25	Primi	9613	V		8.2	0.6	15.1	204	0.074		
eenbanu	22	G2P1L1	5412	V	Pre – H./O PE	6.7	0.9	5.2	190	0.027	Developed Pre-eclampsia	3
ka	19	Primi	1133	V		8	0.7	14.4	186	0.077		

ame	Age	Obstetric Code	IP No.	Socio Economic Status	High Risk factors	Serum		Urinary		UCCR	Outcome
						Calcium	Creatinine	Calcium	Creatinine		
	20	Primi	10317	V		10.4	0.8	17.2	185	0.092	
na ari	26	Primi	9790	V		8.3	0.8	14.7	230	0.063	
	19	Primi	1928	IV		7.2	1.1	6.7	170	0.038	Developed Pre-eclampsia
a	34	Primi	1663	IV		7.6	0.8	13.6	201	0.067	
a	23	Primi	12785	IV		8.5	0.9	14.9	250	0.059	
mi	19	Primi	2195	IV		7.8	0.7	16.5	200	0.062	
eswari	25	Primi	1024	IV		7.9	0.6	12	252	0.078	
na	20	Primi	13176	IV		6.7	0.9	6.2	175	0.035	Developed Pre-eclampsia
akshmi	22	Primi	7642	IV		8.2	0.6	10.9	216	0.050	

	20	Primi	7656	IV		10.6	0.8	16.2	156	0.103	
a	21	Primi	9520	IV		8.4	0.7	15.1	241	0.062	
hitra	23	Primi	4685	IV		11.1	0.7	18.1	180	0.100	
	18	Primi	993			8	0.9	11.2	210	0.053	Developed Pre-eclampsia
	23	Primi	2100	V		10.6	0.7	17.1	198	0.086	
a veni	22	Primi	4680	V		8.2	0.8	14.9	199	0.074	
	18	Primi	970	V		8.2	0.6	15.1	290	0.052	
kshmi	26	Primi	1721	V		8	0.6	16.1	242	0.066	
hi	19	Primi	2159	V		8.6	0.6	15.2	226	0.067	
ni	21	Primi	9715	V		7.4	0.8	13.9	211	0.065	
na	31	Primi	2009	V		6.6	0.9	4.8	150	0.032	Developed Pre-eclampsia
	20	Primi	7738	IV		7.2	0.7	14	196	0.071	
ami	19	Primi	9978	IV		7.8	0.7	14.1	245	0.057	
ani	25	Primi	9986	IV		7.6	0.8	13.2	200	0.066	
wari	29	Primi	9684	IV		8	0.9	14.5	196	0.073	
na	30	Primi	9615	IV		7.9	0.6	12.7	235	0.054	

CONTROL STUDY

ame	Age	Obstetric Code	IP No.	Socio Economic Status	High Risk factors	Serum		Urinary		UCCR	Outcome
						Calcium	Creatinine	Calcium	Creatinine		
	21	G2P1L1	10202	IV		8.6	0.6	16.2	245	0.066	
Selvi	33	G2P1L1	10240	V		10	0.6	18.2	295	0.061	
ri	25	G2P1L1	9198	V		9	0.7	16.1	186	0.086	
mi	27	G2P1L1	10397	V		9.2	0.6	16.9	200	0.084	
ys	26	G2P1L1	1758	IV		7.9	0.6	11.9	185	0.064	
lakshm	22	G2P1L1	1068	IV		7.5	0.6	12.6	176	0.071	
	28	G3P2L2	10263	V		10	0.7	18.2	194	0.093	
i	30	G3P1L1A1	1065	V		8	0.8	15.2	188.	0.080	
udha	34	G2P1L1	9618	V		6.5	1.0	5.9	210	0.028	Developed pre-eclampsia
ri	25	G2P1L1	8950	V		8.6	0.6	15.9	199	0.079	
a	26	G2P1L1	9624	V		8.7	0.6	16.1	176	0.091	
a devi	36	G3P2L2	9769	IV		7.8	0.7	14.2	165	0.086	
na	19	G2P1L1	9706	IV		9.2	0.7	17.1	240	0.071	
mi	24	G2P1L1	9579	IV		9.2	0.7	15.6	195	0.08	
ozhi	30	G2P1L1	2158	V		9.4	0.6	18.2	202	0.090	
a	32	G2P1L1	9494	V		7.9	0.8	15	180	0.083	
a	24	G3P1L1A1	9590	V		6.8	0.9	12.9	184	0.070	
gi	35	G2P1L1	2158	V		7.9	0.7	151	215	0.070	
agavali	25	G2P1L1	1761	V		8.3	0.6	16.8	220	0.076	
hmal	24	G2P1L1	10020	IV		7.9	0.8	13.7	241	0.056	
ala	27	G2P1L1	1782	IV		7.7	1.0	11.5	200	0.057	
ni	20	G2P1L1	10252	IV		8.4	0.6	16.8	224	0.075	
	28	G2P1L1	10205	V		9.6	0.6	18.9	198	0.095	
am	32	G3P2L2	18076	V		10.1	0.6	20.1	188	0.106	
aveni	22	G2P1L1	9509	V		9.4	0.6	19.1	238	0.080	

me	Age	Obstetric Code	IP No.	Socio Economic Status	High Risk factors	Serum		Urinary		UCCR	Outcome
						Calcium	Creatinine	Calcium	Creatinine		
ha	20	G2P1L1	871	V		8.2	0.6	16.8	228	0.073	
a	29	G2P1L1	1165	V		8.4	0.6	14.8	174	0.085	
n	26	G2P1L1	1051	IV		9	0.7	16.1	198	0.081	
a	24	G2P1L1	1376	IV		9.4	0.8	18.3	164	0.111	
ath	19	G2P1L1	994	IV		8.5	0.7	15	186	0.086	
ni	23	G2P1L1	964	V		7.9	0.8	11.8	225	0.052	
	29	G2P1L1	4599	V		11	0.6	19.1	200	0.095	
n	22	G2P1L1	9637	V		8.6	0.7	17.3	203	0.085	
ya	24	G2P1L1	1107	V		9.2	0.8	17.9	250	0.071	
thi	22	G2P1L1	1045	V		9.1	0.8	18.2	201	0.090	
	20	G2P1L1	14962	IV		8.4	0.7	15.4	210	0.073	
hi	22	G2P1L1	14645	IV		8.6	0.7	14.7	175	0.08	
ni	23	G3P2L2	14871	IV		9.1	0.8	18.6	204	0.091	
undari	21	G2P1L1	2102	V		10.5	0.6	19.2	189	0.101	
avathi	25	G3P1L1A1	14820	V		9.5	0.8	17.8	183	0.097	
	23	G2P1L1	1221	V		9.8	0.7	16.9	175	0.096	
	21	G2P1L1	14809	V		8.5	0.6	15.7	204	0.076	
laxmi	31	G3P1L1A1	2083	V		7.5	0.9	12.3	196	0.062	Developed pre-eclampsia
lya	27	G2P1L1	9640	IV		7.9	0.9	11.7	209	0.056	
	22	G2P1L1	258	IV		10.2	0.6	17.2	198	0.086	
chi	23	G2P1L1	1928	IV		9.5	0.7	16.5	208	0.079	
wathi	23	G3P2L2	1103	V		11	0.6	18.8	190	0.098	
a	23	G3P1L1A1	1007	V		8.5	0.7	14.6	174	0.083	
limathi	24	G2P1L1	14810	V		8.1	0.7	7.9	230	0.034	
tha	21	G2P1L1	4586	V		8.6	0.7	14.8	182	0.081	